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# BULLETIN

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# THE JOHNS HOPKINS HOSPITAL



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### JACOB BIGELOW\*—A SKETCH.

By J. G. MUMFORD, M. D., Boston.

The two most conspicuous names in Boston medicine of the last century are those of Jackson and Bigelow. Of the former, this Society heard something a few years since from my friend Dr. Osler. The Jacksons, father and son—the son cut off in his early youth, and memorialized by his distinguished father—fill a unique place in our annals. The Bigelows, father and son, both lived long and active professional lives; their working years covering in all more than eight decades. To the younger generation, the distinguished son, surgeon and teacher, Henry J. Bigelow, is the better known. But I doubt if in future annals his fame will eclipse that of his father.

Recently, we have received a biography of the younger Bigelow from the pen of his colleague, Richard M. Hodges; to me one of the very best medical memoirs known. The story of the *father's* life has never been fully written. Obituary notices, and a brief laudatory sketch by a layman friend we have, and his own writings. From such insufficient data I have attempted to collect and compress into a short paper what little I may of this distinguished man.

What is it that he did? On what does his fame rest? Why do our seniors still name him with respect and almost with reverence?

Men who knew him, tell this of him—He was a wonderful old man. His mind was alert to the very end. He was full of wit, humor and satire. He was wise, acute, profound. He was one of the ablest practitioners we ever had.

But there was more than this in it all. What the man

did impressed enormously the community in which he lived, the source of the impression being often almost unrealized.

The story of his life, briefly and simply related, is a stimulus in itself, and tells us of the development of medicine and scientific thought through many of the transitional formative years of the century.

Jacob Bigelow was born on the 27th of February, 1787, and died on the 10th of January, 1879, nearly ninety-two years old. His life embraced all the greatest events of our Country's history—from the adoption of the Federal Constitution, through the Reconstruction days. And no man more than he grasped the meaning of all that wonderful era. Born at a time of political expansion, he came to know personally all the foremost figures of the age among us. John Adams complimented him, Thomas Jefferson corresponded with him, Daniel Webster was a fellow townsman, Lincoln and Grant were familiar to his riper years; and though with politics he never had active concern, he was always an appreciative student of national development, and in his place was an aggressive and liberal promoter of reforms—municipal, social, educational and scientific.

He was of New England ancestry. His great-great-grandfather came from England about 1640 and settled in Watertown, Massachusetts. In that vicinity the family always lived. His father, Jacob also, was a Congregational minister in Sudbury.

The younger Bigelow's childhood was passed in the country at farmwork and scant schooling. Painfully, his father was enabled to send him to Harvard College, where he was graduated in 1806.

\*Read before the Johns Hopkins Historical Club, October 14, 1901.

During these early years, he was not slow in the pursuit of useful knowledge. Nature always charmed him, and in the study of her mysteries he was an eager scholar. Flowers, the succession of crops, the building of the trees, the changes of the seasons, meant always more to him than to the average, simple, country lad.

In college he was not unknown. In his brief autobiographical notes, which end with his middle life, he tells us that he was a member of a "Theological Society, which was very good; a Porcellian Club, which was very bad; a Phi Beta Kappa Society, intended to be composed of the best scholars; and a Navy Club, which was above suspicion as containing the worst." He was the poet of his commencement day.

Like Astley Cooper, Bigelow had no special "call." Beyond the fact that he had an inborn love of Nature, there was nothing to lead him to scientific pursuits. The choice between law, theology and medicine exercised him not a little, and he tells us that his opinions were at last confirmed by the anatomical lectures of one of the earliest and most forceful surgeons of our country, John Warren.

Were it not for wandering too far afield, it would be interesting here to relate Bigelow's impressions and opinions of that distinguished man, the first of a well-known family of Boston surgeons; for he used often through life to speak in glowing and delighted language of the great fluency and charm with which Warren lectured.

On the choice of a profession, Bigelow has many interesting things to say; and, in his later years, contrasts eloquently the great range of pursuits which became open to aspiring youth, as compared with the narrow things of his boyhood. "Few young men," he says, "would then have cast their fortunes on the uncertain chance of finding occupation and livelihood in the almost unexplored paths since successfully pursued by multitudes of educated aspirants—in the capacities of engineers, mechanical and chemical manufacturers, artists, authors, editors, lecturers and teachers of the higher class. Is it not possible that future learned professions will spring up for the future wants, luxuries and perversities of mankind? Why should not cookery, which caters to the gratification of one sense, take its place as a fine art by the side of music and painting; and why should not a refined and cultivated anaesthesia be so varied in its applications and degrees as to exempt mankind from their griefs and grievances by an artistic application?"

In 1806, the status of medical education in this country was most elementary. Aside from the New York, Philadelphia and Harvard schools, there was no medical college of high standing, and even they offered the shortest of courses to their matriculants. Indeed, it was not until 1810 that Harvard, following the example of the older schools, granted her graduates the doctor's degree.

But Harvard, and a residence in Boston, were beyond the reach of young Bigelow on his leaving college. So one year he spent in Worcester as tutor and student before matriculating in the medical school of his Alma Mater. There the

professors were then but three—Warren, Jackson and Waterhouse.

Bigelow came, then, to Boston in 1808 to attend the lectures of the medical professors, entered as a pupil the office of Dr. John Gorham, and eked out his scanty income by teaching in the Boston Latin School. He became a student of science while continuing to broaden his familiarity with the ancient classics.

One year only he passed in Boston—then to Philadelphia, in 1809, for the lectures of Rush, Wistar, Physick, Barton and Cox, and the doctor's degree.

He was twenty-three years old.

From the very outset, Bigelow showed characteristics familiar enough among American youths—ambition, courage, confidence in himself, adaptability to his surroundings, versatility, a keen sense of perspective, humor in its best sense, and an inexhaustible capacity for work. When funds from home failed him, during his medical course, he took to teaching. To bring himself early before the professional public, he took to writing, and secured the handsome Boylston Prizes in four successive years; indeed, it began to be said that the Boylston Prize was instituted for Bigelow's benefit. Coming to Boston penniless, unknown, without friends or connections, he cultivated from the outset the best among his contemporaries and was an early member of their social, professional and literary gatherings. Among these men, friends of his youth, were: Alexander Everett, a brother of Edward, George Ticknor, H. D. Sedgwick, Nathan Hale, Edward T. Channing and William P. Mason.

So well-known had he become, so promising seemed his career, that within two years the elder James Jackson chose him as his associate in practice. Dr. Jackson had recently been appointed Professor of Theory and Practice at Harvard.

Early there became evident in Bigelow a facility in the handicrafts which was equalled only by his brilliancy in intellectual pursuits. That he gave himself largely to the subjects of therapeutics and internal medicine, has always been an interesting fact. He would doubtless have succeeded as a surgeon, as did his distinguished son. He was a born artist, artificer, craftsman, mechanic and inventor; and there has probably never been a man better equipped by natural endowment for success in all branches of the healing art. So far as appears he never had any regular instruction in drawing or mechanics, but qualified for these pursuits by persistent personal inquiry and the exercise of his natural genius.

When occasion came for illustrating his Medical Botany with colored engravings, and before modern methods of lithographing were invented, he, himself, devised a means of illustration which proved both practical and beautiful. When he wished for drawings and models for his lectures as Rumford professor he knew how to make them. When he was called upon to lay out the plan of Mount Auburn Cemetery, he proved himself an ingenious and practical landscape gardener. He was wont to appear in every workshop, garret and cellar in Boston, where artisans or mechanics would grant

him entrance and answer his questions. He knew what was done and how done by smith, glass-blower, clock-maker, type-caster, printer, moulder and engraver.

At the age of twenty-five, when less than two years in practice, his extra professional activities were punctuated by an election to the Anthology Club—a famous literary body which was founded in 1805, with fourteen members, and after a flourishing existence of many years, developed into that most unique and popular of all private libraries, the Boston Athenæum.

Of course, he joined the Massachusetts Medical Society, and was early honored with an election to the Massachusetts Historical Society, and the American Academy of Arts and Sciences.

In 1812, too, his interest in the study of botany and appreciation of its popular possibilities, led him to give a course of popular lectures on botany in Boston, under the patronage of John Lowell.

Bigelow often said what has been said by many other distinguished and successful men, that a professional man should have a hobby. I suppose his own hobby was botany; though, indeed, he rode many little hobbies besides. At any rate, to botany first he betook himself, in no amateurish fashion, and studied, and lectured, and wrote books. "*Florula Bostoniensis*" was one of them, a volume well-known to our grandfathers; a simple, charming, comprehensible English book, bringing Nature and fields and forests and flowers nearer to simple minds.

Now these studies of the young Bigelow brought him many friends near home and distinguished correspondents from abroad. Such were: Dr. Henry Muhlenberg of Pennsylvania, The Abbé Correa de Serra, at that time Portuguese Minister at Washington, perhaps the best cultivated man in America—kindly, learned, much acquainted, widely known in science. And there were also such correspondents as Sir J. E. Smith, De Fontaine, Jussieu, and de Candolle.

So Bigelow began to be known among the wise men of Europe, when he was not yet thirty, and being no pedant, began to be liked among common folk at home. His practice among them spread, and Harvard College appreciated him and made him a professor.

In 1815 he was appointed lecturer on *Materia Medica* and Botany; and in 1817, when he was thirty, they changed his title to professor, and made him the colleague of James Jackson, J. C. Warren, John Gorham and Walter Channing. He held the chair for forty years.

Many writers have observed that a man's most interesting years are his early, formative years; and novelists have made use of this fact. But it was not altogether so with Jacob Bigelow. While he was poor and young, strenuous and ingenuous, he was an interesting figure; but I hope to show that he remained an interesting figure, rich and old, still strenuous and wise.

To tell much of those early years, there is little time or space. He was a poet, for he read a Phi Beta Kappa poem

at Commencement on the theme "Professional Life" in words somewhat original, in style, Drydenesque.

And while he was doing these intellectual things, his hands were not idle, nor was his tongue backward in telling of his tasks. Of his many-sidedness, perhaps I have said enough, and it will illustrate the "why" of his being appointed Rumford professor and lecturer on the Application of Science to the Useful Arts at Harvard.

He was the first Rumford professor.

Again, were it not for the limits of time, it would be pleasant to say something of that distinguished Count Rumford, and to tell Tyndall's delightful story of his romantic and useful life.

But Rumford was dead, and had left some money to Harvard College for the purpose aforesaid, and Bigelow was appointed to carry out the purpose—a man, I believe, after Rumford's own heart.

This novel bequest of Rumford which established a professorship with an annual income of \$1,000, marks an interesting departure in American university education. It seems to have been accepted by the college with a certain amount of scepticism at first; but the unusual talents and ability of the first professor shed a light upon utilitarian topics which was most unsuspected by the dons of that day.

On the 11th December, 1816, Bigelow devoted his opening lecture to the Life and Works of Count Rumford. The force, sanity, and eloquence of the address, when it came to be printed, met with praise from men of all sorts.

I think that this appointment, and the meaning of it all, came to be for Bigelow the most significant event of his life. Doubtless, the developing science of the last century would have found in him an enthusiastic student under any circumstances. But it is fair to suppose and pleasant to believe, that Rumford, the distinguished American, the idol of foreign courts, the founder of scientific bodies, stimulated and left behind him in his native State a young disciple, who needed only that brilliant and successful example to lead him wisely toward the pursuit of truth.

Of these first lectures of Bigelow, the youthful professor, I can give but slight account. The showing of apparatus and the description of technics lend themselves feebly to the printed page. But we know that the lectures were successful and stimulated a growing demand for the popular demonstration of the elements of science.

To Bigelow, himself, their value was greatest, doubtless, as I have said. He was the first of a line of distinguished men to hold this chair, and is represented in it to-day by Wolcott Gibbs, professor emeritus, and John Trowbridge, the actual incumbent.

Then there was that other pursuit, botany, which, with medicine and technology, occupied his life. The little book on Boston Flora, published in 1814, was popular at once. The subject was so plainly and charmingly handled that the volume had a large circulation among the laity from its first publication. Ten years later, in 1824, a second and very much enlarged edition appeared.

This was only the beginning of his botanical givings forth. The work for which he was early distinguished, which brought him into closest contact with the savants of Europe, and gave him honor in his own country, was the elaborate series of volumes published under the title, *American Medical Botany*.

This treatise purports to cover the ground indicated by its title, in a popular, as well as exhaustive manner, and a special interest in it is the elaborate system of plates, designed and largely executed by Bigelow himself.

These rare volumes impress one strongly with the style and method of their contents; the distinctness, finish and beauty of their illustrations; and the excellence of their appearance in paper and typography, which would make them creditable productions at the present day. Their popularity with the unprofessional reader was enhanced by their author's avoidance of technical terms. Copies are now extremely rare.

Bigelow's eminence as a botanist was recognized also by his being appointed an editor of the first edition of the *U. S. Pharmacopeia*, in 1820, at the age of thirty-three, in association with Spaulding, of New York, Hewson, of Philadelphia, Ives, of New Haven, and De Butts, of Baltimore. In this publication, Bigelow's scheme of simplifying nomenclature was followed, thus distinguishing the *American Pharmacopeia* from that of Great Britain.

In 1817, when thirty years old, Bigelow married Mary Scollay, a daughter of Col. William Scollay, of Boston. They had five children, one of whom was Henry Jacob, famous among American surgeons.

So in the year 1820, we may regard Jacob Bigelow as well launched in his life-work. Though still young, a recognized authority on botany, a distinguished lecturer on applied science, a successful teacher and practitioner of medicine; already approaching the acme of his life-work as a physician, let us believe, though the exact extent of his activities is not entirely apparent.

To one studying the professional conditions in Boston at that day, the burden of incessant practice would appear to have been less onerous than it has since become. Boston was fortunate in a goodly number of eminent doctors, and though fees were small, as we reckon fees, it would appear that all were comfortably supported in that frugal generation. Indeed, as regards many of those well-known men, one is not impressed with the sense of their incessant and over-burdened professional activities, great incomes and the increasing demand for their services, as was the case with their English contemporaries. They seem to have had time for a diversity of interests, and it is for this reason, perhaps, that they have left behind them the reputation for wide philanthropy, good literary and scientific attainments, and respectable scholarship.

In the present day, Boston physicians are not conspicuously public spirited. Tradition says that in this they have degenerated. However that may be, and whatever the cause, in Jacob Bigelow we have a conspicuous example of

the reverse. Through life, he was eager and forward in many public movements; in some of them an originator and leader. As with most men, the story of his life falls naturally into three chapters—development, maturity, and age. In all, except the last, he was precocious. For this reason his activities covered a multitude of years. We have traced him through the first chapter. Let the second chapter begin at the age of thirty-eight, and be ushered in with the inception of his first conspicuous public service—the founding of Mount Auburn Cemetery.

Up to this time, 1825, the dead of our cities had been buried in the city church-yards and vaults, and the problem of their disposal was becoming an urgent and a distressing one. With the increase of population, the ground was becoming encroached upon, at the same time that the burials were becoming more frequent. Many of the older church-yards had long been full. Interments were made in graves already occupied, and ancient bones were being disinterred and removed. Shocking as all this was to the sensibility of the community, the danger to the public health was becoming still more serious.

All this had long been a matter of grave concern to Bigelow, and in this year, 1825, he called together at his house a small company of prominent men to discuss the situation and its remedy. He proposed to them a plan which met with their cordial approval, though when it was made public, it was received with a storm of opposition and ridicule.

Bigelow's proposition was the founding of an extra-urban forest cemetery. In a delightful and convincing series of papers, he pointed out the reasonableness of this plan, and the offence of the existing methods. The arguments he used are familiar enough to us to-day. Little was needed to show the disadvantage of past conditions and the advantage of returning bodies to a virgin soil where rapid decomposition in a forest garden might go on unchecked. This was told graphically and strikingly.

For seven years the debate went on, until in 1832, in spite of constant and powerful dissent, the cemetery at Mount Auburn was dedicated for public use. The place is situated in a piece of woods about a mile from Harvard College, on the banks of the Charles, and had long been a favorite resort for lovers of nature. The students had named it "Sweet Auburn."

In every sense, Dr. Bigelow was the founder and promoter of this first modern cemetery. He laid out the grounds; he thinned the trees; he surveyed roads, paths and hedges; he supervised its ornamentation; he designed its classic gateway and approach. For it, indeed, he became the first of our landscape architects.

The success of the new plan was instantaneous and pronounced. From the very opening of the cemetery, it appealed to the sentiments as well as to the reason of our people; and numberless imitations were promptly projected in all parts of the country. As long as he lived, Bigelow continued an active support and director of this work.

In 1872, forty years later, he planned and presented to the trustees the famous Mount Auburn Sphinx—a memorial to the Union Soldiers of our Civil War. It bears this inscription:

America conservata  
Africa liberata  
Populo magno assurgente  
Heroum sanguine fuso.

The year 1832 was marked by the outbreak of a great cholera epidemic in this country. The disease raged fearfully in many of the seaboard towns. In New York alone, three thousand died—the city was almost deserted by the terrified inhabitants. Those must have been very stirring days, if we can believe even the colorless recital of Bigelow's biographer.

Early in the epidemic, and before it had reached Boston, the authorities there determined on vigorous measures for the protection of the city. A strict quarantine was enforced, and a number of eminent physicians were invited to investigate the New York conditions. It is stated that some of those who were asked to take part in this work found reasons for declining; but Bigelow, Ware and Flint willingly offered their services and went as commissioners to the stricken city.

The conditions they found there were said to beggar description. Brockden Brown, in his pompous but luminous pages, tells the story of an earlier visitation; and the same was true in this year of 1832—terror everywhere—deserted streets, crowded hospitals, frightened attendants, and devoted physicians. It was, indeed, such a plague as was known to the Italy of the Middle Ages. The Boston physicians saw and reported. They visited the hospitals; they conferred with the authorities; they studied the cases, and they found a state of affairs far worse than rumor had pictured.

Their mission ended, they returned home, through some difficulties, we are told; for local authorities refused them passport. They were actually turned away from the City of Providence and forced by a circuitous route to make their journey to Boston.

So grievous is their report said to have been, that the Mayor of Boston withheld it from publication for fear of alarming the community; but their recommendations were of the greatest value; and through their efforts, the disease was largely averted from the town; the mortality figures showing that while New York lost three thousand by death, and many other seaboard cities between one and two thousand, the Boston deaths were but one hundred in all. \* \* \*

It seems as though, with the approach of middle age, Bigelow had already accomplished a good life-work. Indeed, he himself seems so to have thought. In 1833 he was forty-six years old, and felt himself to have earned a rest from his constant labors. In this year, then, he went to Europe for the first time—a mature man, famous in his own country, and already well known to foreign scholars. One of his companions in this voyage was the young O. W. Holmes, his

pupil, a recent graduate in medicine, going to Paris to complete his education.

With this voyage ends the story told in Bigelow's modest autobiography.

Beginning with this second era, his middle age, Bigelow's activities continue in many new directions. He was visiting physician to the Massachusetts General Hospital. He was professor of *Materia Medica* at Harvard. He conducted an enormous consulting practice. He was a very frequent contributor to the press on matters of public interest. He was chairman or trustee of many important public and private organizations. But above all, he became conspicuous for the great reforms which he instituted in the practice of medicine.

Mount Auburn will always remain a permanent monument to Bigelow, the citizen. But the physician's work as a pioneer in science should, and I believe will, give him a more permanent place in our annals.

At the outset of his professional life, he was imbued with the prejudices and traditions of the so-called heroic method. He had been taught that the department of therapeutics was the most important in medical practice. This was the belief of all the world at that time, and with few exceptions physicians regarded the study of disease, the careful review of etiology, the course and nature of symptoms, the appearance of morbid processes, and the proper estimate of prognosis as very secondary matters.

To be sure, there were rising in France and in England a few men who were beginning to appreciate the value of observation; and the statistical method, rather than the study of individual cases, about this time had its inception. But such work, and especially that of Louis in Paris, as yet was little known.

In our own country, medicine had advanced but little beyond the teaching of the 18th century, and with the exception of Jenner's vaccine, we were still in darkness.

Very early in his career, and influenced by his interest in and pursuit of science in broader fields, Bigelow was led to a habit of observation and just conclusion. He came to see that disease is by no means susceptible of ready curtailment; that great numbers of processes run a definite course, with spontaneous recovery; that other processes subside and recur periodically; that others still persist to the end uninfluenced by therapeutic measures; and that there is underlying it all a *vis medicatrix naturae*, too little reckoned with.

In those early days, too, when ingenious men were advancing theories founded on speculation and insufficient observation; when text-books were loaded with *ex cathedra dicta*, dogmatic teachers were looked up to by the public and medical students as almost divine healers. The teaching of Hahnemann, and the wide enthusiasm of his followers in homœopathy had led great numbers of persons to regard the ancient methods as humbug; and many educated men were being led away into these new practices. Bigelow saw clearly and pointed out the significance and meaning of it all. His voice was heard in the land, and for many years,

in season and out of season, he ceased not his demonstrations of the self-limited character of disease.

All of this is now so trite and so familiar even to the intelligent among the laity, that it seems a little thing. But the daring of it and the success of the pioneer in those days were very heroic and real.

In 1835, in an address on "Self-limited Diseases," before the Massachusetts Medical Society, Bigelow struck the true note; the effect was instantaneous and immense.

In popular opinion, homœopathy has the credit of inciting and furthering that radical change in the methods of medical practice which has now prevailed among us for two generations. Quite otherwise is the truth. Writing in 1880, Dr. O. W. Holmes says in reference to this address of Bigelow: "This remarkable essay has probably had more influence on medical practice in America than any similar brief treatise, we might say than any work ever published in this country. Its suggestions were scattered abroad at the exact fertilizing moment when public opinion was matured enough for their reception." \* \* \* \* \*

In 1852, Bigelow delivered before the students of the Massachusetts Medical College in Boston, a striking address on medical education, the key-note of which was similar to that of his famous essay on Self-limited Diseases; at the same time he urged upon his students the great importance of a thorough scientific training. This was twenty years before that beginning of reform in medical education in America which was initiated by Harvard some thirty years ago. The trend of Bigelow's remarks was in the line of those better things with which we are now familiar.

He naturally deprecated the vicious practice of that day which allowed students to qualify for the degree after two short courses of lectures and a certain amount of practice in the offices of physicians. But he went much further than merely urging that three and four years' course of medical study with which our generation is familiar; he anticipated and advocated that development of special instruction to which to-day we are turning.

Didactic lectures in themselves he recognized as useful and important; but original research on the part of students, and personal investigations in laboratories, in small classes, under supervision of competent instructors, he advocated as most important of all. His views on this subject coincide with those of the leading scientists of modern times, and it has interested me lately in reading Huxley's biography, to see how 40 years ago that great man insisted upon the personal, as distinguished from the second-hand methods of study.

Bigelow then went on in his characteristic style to define the exact sciences and the speculative sciences; pre-eminent among the latter he places practical medicine—"a science older than civilization, cultivated and honored in all ages, powerful for good or for evil, progressive in its character, but still unsettled in its principles, remunerative in fame and fortune to its successful cultivators, and rich in the fruits of a good conscience to its honest votaries. Encumbered as it

is with difficulty, fallacy and doubt, medicine yet constitutes one of the learned professions. It is largely represented in every city, village and hamlet. Its imperfections are lost sight of in the overwhelming importance of its objects. The living look to it for succor; the dying call on it for rescue."

He proceeded more elaborately to explain the difficulties of therapeutics, using the old-time comparison between the physician and the experienced pilot, and showing that the rocks and narrows in the pilot's course must be known to him, this knowledge being of far more importance for the safety of his bark than his ability to calm the winds and the waves.

And so he comes to the inevitable conclusion—for us now the last word—"That he is a great physician who above other men understands diagnosis."

This charming essay, intended for young beginners; lucid, free from technicalities, can be read by any layman, and is indeed a very missionary tract.

These two essays, and a number of others on medical and general topics—homœopathy, quackery, burial of the dead, pneumo-thorax, tea and coffee, the history and use of tobacco, etc., etc., are bound together in a little volume, entitled "Nature in Disease, and Other Writings." Published in 1854.

In the last generation, this book was to be found on the shelves of every well-equipped library in New England. Simple and unpretentious, its influence inside and outside the profession was immense, and I believe to it, more than to the writings of any other one man, we owe the appreciation and popularity of the medical profession in this country.

In such studies and pursuits, then, we must believe that Bigelow immersed himself for the many years of his long middle age.

Of his private life there is no space to tell, nor of his connection with the stirring events preceding and accompanying the Civil War.

Side glimpses of him we have in the records of medical societies of those days; notice of his constant attendance at such meetings; and quotations from his strong, wise and earnest sayings. In those years, his son, Henry J. Bigelow, was coming rapidly to the front as teacher and practitioner of surgery; and when we come down to the Civil War days, both of these men, father and son, were already past military age, so that their public labors in those trying times were little associated with the activities of camp and battle.

The high patriotism of the elder man, we know; for is it not evidenced by that monument which he, himself, designed?

\* \* \* \* \*

Now with the war days began the third era in Bigelow's life—his old age. Still useful, still forceful, his endeavor was constant for the intellectual uplifting of his fellows.

Throughout his long career, his utilitarian studies, his contact with eminent scientific men of all countries, and his abundant experience as a practitioner of medicine had confirmed him in the belief that the old-time pursuit of the classics, the traditional "liberal education," was for success

and usefulness in life by no means salient. Indeed, he had convinced himself that in our days a liberal education means far more than an intimacy with the ancient classics; and this, too, in spite of his own high training and accomplishments in that branch of learning.

With such convictions, Bigelow took a profound interest in the Massachusetts Institute of Technology, which was incorporated in the early days of the Civil War; and at the dedication of its new hall, on the 16th November, 1865, he delivered a striking address on the "Limits of Education." His object was to break, or rather to extend, those limits in a way to make education "conduce most to the progress, the efficiency, the virtue and the welfare of men."

This address is so striking, so in advance of the times, so complete, even for us to-day; so little has been added to it by more recent thinkers, that it is difficult to pass it by without quotation.

The early training of a pupil must be as thorough as possible; "but after this is completed, a special or departmental course of studies should be selected—such as appears most likely to conduct him to his appropriate sphere of usefulness. Collateral studies of different kinds may always be allowed; but they should be subordinate and subsidiary and need not interfere with the great objects of his especial education."

"A common college education now culminates in the student becoming what is called a master of arts; but this, in the majority of cases, means simply a master of nothing."

He assigns much of the modern conditions among us to English conservatism, for the conservation of a privileged order—"It is the duty of educational institutions to adapt themselves to the wants of the place and time in which they exist."

"Life is no less short now than it was for the Roman poet, but art is vastly longer."

Such earnest thoughts as these were much in Bigelow's mind, and he carried them soon to the American Academy of Arts and Sciences, over which he had long presided.

In his address before the Academy the next year, he developed the same theme; realizing the immense demand of this expanding country for the services of expert, educated men—"in its cities and mining regions and factories and workshops; for skilled labor, for chemists, engineers, architects, constructors, overseers."

A great antagonism was aroused, but the majority of critics were friendly.

Out of this turmoil, and especially out of a challenge on the arena of the academy, came a further reply from Bigelow. His biographer describes the scene from memory—a social meeting of the Academy at Bigelow's house, on the evening of the 20th of November, 1866. The title: "On Classical and Utilitarian Studies."

This paper was the longest, the most elaborate and the most learned of his written productions. Of it, his biographer says—"The sparkle and brilliancy of its style, the exuberance of its playful humor, the keenness of its occas-

ional satire, the compass and wealth of its scholarship, the cogency of its accumulating argument and demonstrative affirmations may claim for that essay a very high distinction among the masses of our recent like productions."

The pith of his argument is this; and it is the argument underlying the whole trend of modern democratic thought: That education is the right of the many and not the privilege of the few; that that conservatism which restricts education to the classics and what may be called aesthetic culture is but the highest form of class-selfishness; that such practices are not only in themselves vicious, but tend to the lowering of the whole educational fabric; that the underlying thought in education is the teaching how to *think* and the meaning of *study*; and this much at least is due to the masses; that it is those things which tend most to the useful arts, to the alleviation of human suffering, to the broadening of the popular horizon, for which we must all strive. All this, trite enough to us in these days, was not an old thought thirty-five years ago, even to the distinguished scholars who formed his audience; and the teachings of Froebel had not yet been accepted among us here.

Then, glancing rapidly back, Bigelow said: "The wisdom of the ancients was selfish in its privileges, inwrought with error, superstition and vice; confined to a very few; inoperative and useless to the masses; it did not and could not advance any vast public and improving interests, nor conserve social prosperity and order."

Speaking of the Renaissance, he remarks in a paragraph full of interest, that the popular idea of this brilliant epoch as a revival of classical learning is untrue. That the study of the classics was but one evidence of the reviving and wide-spread interest in intellectual pursuits. Literature, the arts, science, all shared equally in the new advance; and of them all, science soon began to cut for itself a broad, new and straight path.

How large an influence these discourses of Bigelow had upon modern thought and purpose, it is difficult to say. Doubtless, he was one of many; but to me the interesting thing is this: that such teaching, vigorous, forceful, forward, was but the continuation of the lessons of a long life; for eighty years he had been a modern. Grasping the meaning of science in his youth, he had held it steadily before him. And now we see him nearing the end of his career, preaching and teaching among the most radical thinkers; ancient as he was, leading the advance in the great educational reform of our time. Never senile, never looking backward, but always confident of better things to come.

These educational essays caused widespread discussion, both at home and abroad, when they came to be distributed. The historian, Lecky, wrote from Italy a strong and interesting letter of dissent; but Lyell, Huxley, Spencer and other liberal Englishmen were vigorous in their commendations. The essays under the title "Modern Inquiries" were published at the time of a forward educational movement in England.

Lyell writes to Bigelow: "Our universities and all the

principal schools are as you know, in the hands of the clergy; hence we shall have more difficulty than you in introducing the elements of science and natural history. The clergy: Romanist, Anglican and Dissenting, have hitherto proved too strong for us. Reformers and American and continental rivalry must be brought to bear before we shall succeed. Your book will be most useful at this moment in this country."

"By their fruits ye shall know them" is sometimes true. It is true at least in Bigelow's case; for I believe it is fair to say that the Massachusetts Institute of Technology, with its splendid curriculum, its strong staff, its host of highly trained and successful graduates, stands to-day a monument, in part at least, to the energies of this distinguished man.

That work for educational reform was Jacob Bigelow's last great work. He did many other things in his declining years; pleasant things, to be remembered by his friends. He became the old-man Oracle—a Nestor most distinguished, most approachable; of whom one hears to-day nothing but

good. It was a busy old age, given for a time, more than is the wont with Nestors, to travel and intercourse with men. When eighty-three, he went to California, a pleasure trip, with wife and friends; and of the wonders there he explored many.

In old age, too, he amused himself much with playful writings, extra-professional, the best known of which was *ΧΗΝΟΔΙΑ* "Chenodia"—a classical Mother Goose, the ditties of that good dame rendered into Greek and Latin.

A pretty collection is *Διάφορα Ποιήσεις* (Various Poetry), a volume of fugitive, humorous poems, attached to which are the names of well-known writers, his friends; Bryant, Longfellow, Holmes, Emerson, Lowell and others.

In such and other pleasantries he passed his declining days—not in harness, a garb scarce suited to ninety-two. Blind at the last, for nearly five years. Bedridden, but with mind undimmed. Much sought out, even so. Unforgotten to the very end, though long inactive among us. The story fades away gently—the history remains.

## PROPER FOOT WEAR AND THE TREATMENT OF WEAKENED AND FLAT FEET BY MECHANICAL DEVICES FOR MAINTAINING THE ADDUCTED POSITION.\*

BY JOHN A. SAMPSON, M. D.,

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In studying the feet of a child who has never worn shoes or stockings, we are impressed with the fact that we have not inherited the acquired characteristic of deformed feet. For the foot of the infant is practically normal. The long arch may seem flatter than it should be, but Dane<sup>1</sup> has shown by serial sections of the feet of infants that the apparent flattening is due to a pad of fat, which acts as a brace until the foot becomes stronger. In the feet of poorly nourished infants the long arch is very apparent, for this pad is absent.

This arch may be divided into an outer one, which is low and only slightly yielding and well adapted to continuous weight bearing, and an inner, which is higher and much more elastic. The latter is the one usually spoken of as the long arch. Both arches are permanent. The outer is affected very little by the movements of the foot, while the inner is lowered by some movements and deepened by others. During action the arches are relieved from much of the strain by the muscles of the leg and the foot, while in the passive support of the body weight, as in standing, more of the strain falls on the ligaments.

The transverse arch is not permanent. It flattens out when the body weight is thrown forward, thereby widening

the front of the foot so that we may walk with greater surety. It reforms as soon as the weight is removed. It is lessened by dorsal flexion of the toes, and increased by plantar flexion. These arches impart ease and elasticity to all our movements and relieve the body of the jar which would otherwise be caused by the transmission of the body weight to the ground. By maintaining their structure and position the various forms of work to be done are distributed to the parts of the foot best adapted to that work. Thus the foot may be used to its best mechanical advantages.

If one grasps the foot firmly with one hand to restrict motion between the os calcis and astragalus, and with the other pushes the front of the foot towards the median line, motion taking place mainly at the mediatarsal joint, the foot becomes adducted and shorter. There is a slight elevation of the inner border, the edge of the outer border becomes more convex, and associated with these movements the long arch is deepened.

The forces causing adduction of the foot, as represented in Fig. 1, may be resolved into three (1, 2 and 3), and are the same one would use to bend a stick into a similar position, the angle being formed at the mediatarsal joint of the foot. The angle *abc* in Fig. 1 is indicative of the amount of lateral deflection of the front of the foot and is determined as described by Roberts.<sup>2</sup> On an impression or outline of the foot a transverse line is drawn corresponding

\* Read at the Johns Hopkins Medical Society, October 21, 1901.

<sup>1</sup> Further Studies upon the Arch of the Foot in Infancy and Childhood, Trans. American Orthopedic Association, vol. xi, 1898, p. 61.

<sup>2</sup> Contributions to Orthopedic Surgery, pp. 217 and 218. Phila., 1898.

to the mediotarsal joint (*J*) and perpendicular to it a line corresponding to the long axis of the os calcis (*a, d*). Another line is drawn through the head of the 1st metatarsal bone, to the intersection of the other lines (*c, b*). The angle formed by this and the perpendicular line we may call the angle of lateral deflection. If we reverse our forces, as shown in Fig. 2, abduction takes place, the foot becomes straighter and longer, the angle of lateral deflection less, the outer border slightly elevated and nearly straight with these movements the long arch is lowered. A very simple way of demonstrating these associated movements is to construct a model out of strips of cardboard which have been bent to represent the arches and fastened together with McGill fasteners, as in Fig. 3. *CAD* represents the inner portion of the long arch and *CBE* the outer portion. *AB* is the mediotarsal joint. In assuming the adducted and abducted positions the front of the foot moves as a whole,

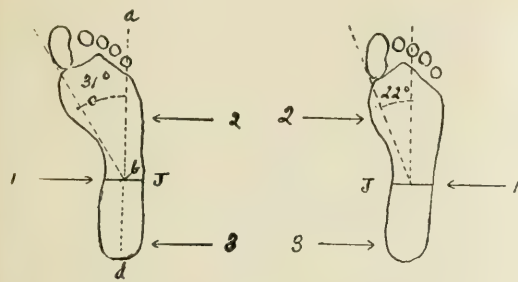


FIG. 1.

FIG. 2.

Fig. 1. Foot in adducted position.  $31^\circ$  angle of lateral deflection. *J* mediotarsal joint. 1, 2 and 3 are the forces one would use to maintain the foot in this position.

Fig. 2. Foot in abducted position.  $22^\circ$  angle of lateral deflection. *J* mediotarsal joint. 1, 2 and 3 are the forces one would use to maintain the foot in this position.

but for the sake of clearness I have represented the association between the anterior portion of these arches by a strip of cardboard, *BD*, and the transverse arch by another strip, *ED*. If the inner arch could move unhampered, the point *D* in assuming the positions of adduction and abduction, would move along the arc 1-2 with *AD* as the radius from the centre *A*, and the height of the inner arch would not be affected by this movement. But the inner arch is high and elastic while the outer arch is lower and much more rigid, and the front of the foot moves as a whole, which means that the strip *BD* is a rigid tether and *D* in assuming the adducted and abducted positions, must move along the arc 3-4, which is formed by *BD* as the radius from the centre *B*. As the inner arch is elastic it will adapt itself to this tether and be shortened and elevated in the adducted position, and lengthened and lowered in the abducted position. All connections between these two arches which we

may construct will confirm the above, that is, that in all movements the inner and elastic portion of the foot must adapt itself to the movements of the outer and more rigid portion. In studying a skeleton of the foot which has been so articulated that the normal motion at the mediotarsal joint has been maintained we can see that in adduction the scaphoid slides under and lifts up the astragalus, that is, raises the arch, and in abduction pushes it down, *i. e.*, lowers the arch. On assuming these positions in standing we readily see that in the adducted position the body weight is thrown to the outer side of the foot over the outer portion of the long arch, which is well adapted to receiving it. This position is one of strength and muscular support. While in the abducted position the body weight falls to the inner side of the inner portion of the arch, causing the foot to be rolled over inwards into a position of weakness and ligamentous support.

Both positions are physiological, as in walking along the

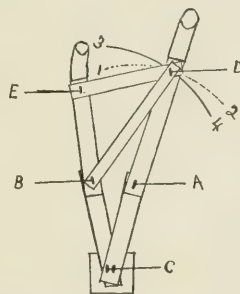


Fig. 3. Schematic representation of the mechanism of the foot, made of strips of card board bent to represent the arches and fastened with McGill fasteners. *CAD* = inner and *CBE* outer portion of long arch. *BD* = rigid tether joining the two portions of the arch. *AB* = mediotarsal joint. 1-2 = arc along which *D* would move with *AD* as a radius. 3-4 = arc along which *D* must move with *BD* a rigid tether as a radius, the arch *CAD* being elastic will permit it.

side of a hill the upper foot will be abducted and the lower adducted, also in walking over uneven ground these positions enable the foot to adjust itself as needed. The abducted position with pronation is the one normally assumed when the body weight is thrown on one foot or both in such a manner that equilibrium is maintained without muscular exertion. This becomes pathological when excessive or used in other or all attitudes. The big toe, by its ability to become adducted (motion towards the median line of the body), aids in supporting the long arch and in preventing the rolling over inwards which occurs in the pronated foot. I wish specially to emphasize that the adducted position of the foot is a natural means of supporting the long arch, and adduction of the big toe is also an aid. A deformity of the foot frequently has two effects; first, the function of that part is impaired, and secondly, by a change in the directions or elevation of the arches, the various forms of work are

distributed to parts ill adapted to that work. The foot must then readjust itself as best it can to the deformity.

#### STOCKINGS.

On observing the feet of adults we must admit that either the inheritance of acquired characteristics comes late in life, or else there must be some other factor in the etiology of deformed feet. Stockings, such as are usually worn, are interchangeable and have pointed toes. During infancy and childhood stockings have more influence in moulding the foot than later, but even in the adult the effect is considerable. If we make tracings of the foot in such a stocking, first with the foot just resting on the floor, then bearing the body weight and compare them with similar tracings of the foot without the stocking, it is evident that the stocking compresses the toes, and not only interferes with adduction of the big toe, but even holds it in a position of hallux valgus. The above is well shown in a series of skiagraphs of feet with and without stockings by H. A. Wilson.<sup>3</sup>

The effect of the hallux valgus and interference with adduction of the big toe is that we have lost a natural means of supporting the long arch and preventing pronation of the foot. Also in walking, in the final push, instead of stepping squarely off from the end of our big toe we walk off from the side, thereby losing some force and also pushing the foot into a position of abduction. Our gait, which should be with feet parallel, now is with adducted and everted feet.

A hallux valgus thus acts not only as a deformed member, but also causes the whole foot to work under disadvantages, and may be considered an etiological factor in the causation and maintenance of the weakened and flat foot.

#### SHOES.

As for the shoes of adults, one would never think of wearing the right shoe on the left foot, but how about the shoes of children? They are frequently interchangeable, and when not, the difference is very slight, the shank being cut away a little more on the inside and the shoe only slightly adducted. The inner edge is not straight enough and there is not enough room along the inner side for the foot to assume the adducted position.

Many adults still wear shoes which cover the feet without much wrinkling and are long enough to extend beyond the end of the big toe, but the shoe was made over a last formed according to the demands of fashion and not to those of the foot which is to wear it. The proper shoe should maintain, or at least permit the foot to assume, within the shoe its position of greatest strength, namely adduction.

In Figs. 4 and 5, I have represented the relations of the proper shoe to a normal foot. The parallel lines indicate the forces which act when the shoe is made to fit the foot

in the adducted position. XY represents a cross section of the foot within the shoe taken at AB.

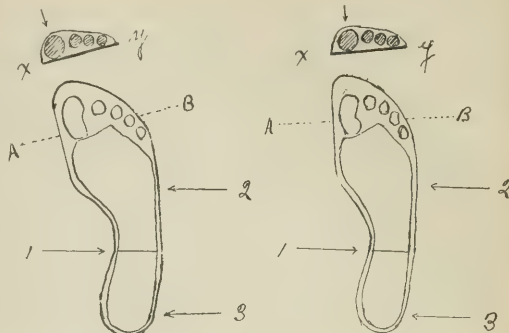


FIG. 4.

FIG. 5.

FIG. 4. Shows the proper relation of the sides of the shoe to the sides of the foot, in a foot which, when voluntarily adducted, the angle of lateral deflection is  $31^\circ$ . 1, 2, 3 are adducting forces caused by the shoe fitting the foot in this position. xy represents a cross section of the shoe, and the foot taken at AB, the deepest portion of the shoe corresponding to the thickest portion of foot, and is along the inner edge.

FIG. 5. Shows the proper relations of the sides of the shoe to the sides of the foot in a foot which, when voluntarily adducted, the angle of lateral deflection is  $24^\circ$ ; otherwise as in Fig. 4. This shoe would not fit the foot in Fig. 4, because the angle of lateral deflection is different and vice versa. The shoe must have the same angle of lateral deflection as the foot.

The deepest part of the front of the shoe corresponding to the thickest part of the front of the foot is along the inner border. In such shoes there is room for the foot to

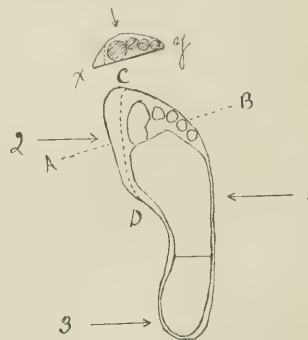


FIG. 6. Shows the effect of a shoe, otherwise correct, in which the deepest portion of the front of the shoe as represented in cross section xy taken at AB is in the middle, and not along the inner edge as in Figs. 4 and 5. The inner side of the foot being thickest will occupy the deepest portion of the shoe, hence the foot represented in Fig. 4 would be abducted in the shoe in Fig. 6. DAC represents the unavailable portion of the shoe. 1, 2 and 3 are the abducting forces.

<sup>3</sup> An X Ray Demonstration of Some of the Effects of Shoes and Stockings upon the Human Foot. Phil. Med. Jour., Jan. 6, 1900, vol. v., pp. 38-39.

assume the adducted position and the big toe is not forced into a position of hallux valgus. Should the deepest portion of the front of the shoe be in the middle, as represented in Fig. 6, even though the rest of the shoe might be correct, the foot would not be able to assume the adducted position and would be forced to the outer side of shoe. This would cause pressure on the smaller toes and the big toe would be abducted. The unavailable portion of the shoe would be as represented by the space *DAC*. A foot having an angle of lateral deflection of  $31^{\circ}$ , when adducted as in Fig. 4, would be held in the abducted position as indicated by forces (1, 2 and 3) Fig. 6.

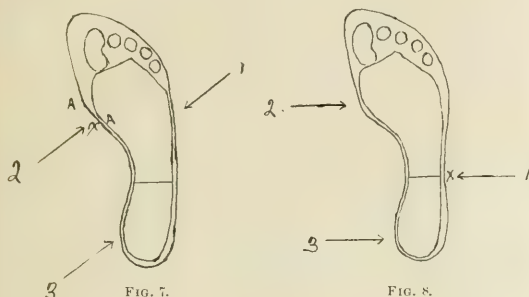


FIG. 7. Shows the effect of a shoe otherwise correct in which the distance corresponding to that from the heel to the distal end of the first metatarsal bone is longer in the shoe than in the foot. The foot is pushed into the abducted position. The point of pressure is indicated at x. A and A' are the points in the shoe and the foot which should correspond. 1, 2 and 3 abducting forces.

FIG. 8. Shows the effect of a shoe otherwise correct which causes pressure along the outer border at x by being concave instead of convex as in Figs. 4 and 5. This pressure pushes the foot over to the inner side of the shoe, but in the abducted position. 1, 2 and 3 are the abducting forces.

In Fig. 7, I have represented the effect of a shoe whose shank is too long from the heel to the position of the distal end of the first metatarsal bone. This also forces the foot to assume the abducted position.

Should a shoe, otherwise correct, have the outer border concave instead of convex at the mediatarsal joint, the inner portion of the foot would be forced into the inner border of the shoe out of the correct adducted position. The forces of abduction are indicated in Fig. 8.

Shoes such as all of us have worn and many of us still wear, may be divided into narrow-toed, and broad-toed, the so-called common sense shoes. The narrow-toed shoe usually holds the foot in the abducted position, being an abducted shoe, or having features in it which prevent adduction. The front of the shoe cramps the front of the foot, the toes are huddled together and the big toe is held in a position of hallux valgus. The available space within the front of the shoe is less than indicated by the outline of the shoe, and the deepest part of the front of the shoe is in the middle,

thus increasing the abduction and hallux valgus already present (see Fig. 9). *DAC*, the unavailable space, would cause one to think that the shoes were not too narrow, for the foot does not fill the shoe.

The so-called common sense broad-toed shoe is usually also an abducted shoe; the deepest part of the front of the shoe, as in narrow-toed ones, is in the middle. Since the thickest part of the front of the foot is along the inner border and as hallux valgus and the abducted position are easily assumed, the foot is forced to occupy the position of least resistance. In the broad-toed shoe there may be very little more available room than in the

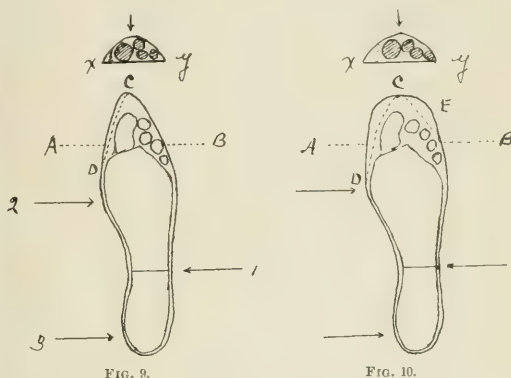


FIG. 9. A pointed toed shoe holds the foot in a position of abduction, compresses the front of the foot and causes hallux valgus. xy cross section at AB shows that the deepest portion of the front of the shoe as in Fig. 6 is in the middle, thereby increasing the abduction and hallux valgus. CAD unavailable portion of shoe caused by deepest portion being in the middle and not along inner edge. 1, 2 and 3 indicate abducting forces.

FIG. 10. So-called common sense shoe holds the foot in a position of abduction, does not compress the small toes as much as the narrow toed shoe. xy cross section at AB shows that the deepest portion of the front of the shoe as in Fig. 9 is in the middle, thereby increasing the abduction and hallux valgus. DAC represents the unavailable space, CEB the unused space. Effect of this shoe on the foot, as shown by dotted lines, is much the same as in Fig. 9.

narrow-toed shoe, as indicated by dotted lines Fig. 10. The broad shoe is more sensible in that there is less compression of the smaller toes and walking is easier, but otherwise its effect on the foot is similar to that of the narrow-toed shoe. Aside from bunions, corns, ingrowing toe-nails, etc., which improper shoes cause, they either hold the foot in the abducted position or hinder or prevent adduction, so that the abducted position may become habitual and cause hallux valgus.

Another feature common to nearly all shoes is the "spring" or dorsal flexion of the front of the shoe which shoemakers introduce so that as the individual walks there will not be any wrinkles in the shoe (see Fig. 14). A per-

son with shoes so formed, as shown by Whitman,<sup>4</sup> rocks off from the end of the foot, the downward force of the toes in walking is interfered with or completely lost, depending on the amount of spring and the thickness of the sole. The downward force of the big toe, as given by Bradford,<sup>5</sup> is 20 pounds in the adult, enough to be considered in the final push of the foot. Dorsal flexion also means lowering or loss of function of the transverse arch. Another fault of nearly all lasts is that the forepart is convex on the bottom from side to side, which means that the inner sole of the shoe will be concave. The body weight will tend to reverse the transverse arch resting in a concave surface already lessened or destroyed by dorsal flexion. People frequently say, their shoes are a little uncomfortable at first, but as soon as they are broken in they do not cause discomfort. One must bear in mind that a shoe is never broken in without breaking in the foot.

### THE HEEL.

In considering the transmission of the body weight through the foot to the ground, we may compare the foot to

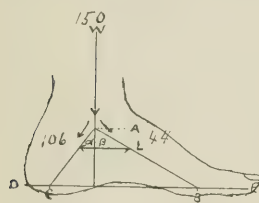


FIG. 11.

FIG. 11. Normal arch  $96^\circ$ ; post. limb 7 and ant. limb 11 cm. long. Body weight  $W = 150$  lbs. Posture erect, standing on one foot directly over the long arch. By mathematical calculations about 44 lbs. would be transmitted along the ant. limb A B and 106 lbs. along the post. limb A C. Strain on the ligaments at L is about 230 lbs.

FIG. 12. Shows what the effect of a heel would be placed well back, so that the posterior limb is lengthened without changing the working angle of the arch. 4 cm. has been added to A C making  $A'C' = AB$ . An equal amount of weight will be transmitted down each limb, namely 75 lbs., an increase of about 30 lbs. on the anterior limb which we know is not as well adapted to receiving it as the posterior limb. The strain on the ligaments at L is about 250 lbs., an increase of about 20 lbs. over the strain in Fig. 11. As shown by angle  $E'BE'$  the toes are held in dorsal flexion.

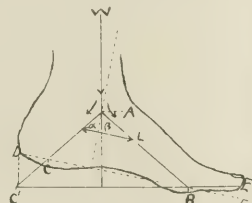


FIG. 12.

extending from the same point to the distal end of the fifth metatarsal bone, are longer, more elastic and better adapted to balancing the individual and giving spring and elasticity to the gait than of receiving a steady strain. For the purpose of obtaining some idea of the amount of strain on the ligaments of the arch and the relative proportion of the body weight transmitted along each limb, let us resolve the two anterior limbs of the tripod into one, or better, consider the inner portion of the long arch.

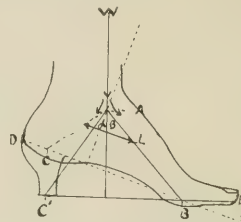


FIG. 13. Shows the effect of placing the heel forward so that it does not form a direct continuation of the posterior limb. The posterior limb is lengthened and drawn forward, thus diminishing the working angle of the arch. The strain on the ligaments at L is less than without a heel, for the working angle is less; the amount of body weight transmitted down each limb approaches the same as the length of the limbs do, the greater amount being transmitted down the shorter limb.

Not being able to find just what I wished in the literature, I measured the angle of this arch and the length of the anterior and posterior limbs in the feet of 25 men whose feet were practically normal. I found that the angle varied from  $95^\circ$  to  $110^\circ$ , the anterior limb from 10 to 12 cm., and the posterior limb from 6 to 8 cm. We will suppose that the individual weighs 150 lbs. and is standing on one foot so, that the body weight falls directly over this arch.

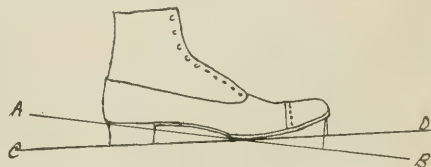


FIG. 14. Shows the "spring" in a shoe which holds the toes in dorsal flexion, thus lowering or destroying the transverse arch. A person with such a shoe "rocks" off from the end of the shoe. Viewed from the plane, A B on which the entire foot should rest, we can see that the heel has doubled the "spring" or dorsal flexion of the front of the shoe.

In Fig. 11 I have represented the arch of a person weighing 150 pounds, angle being  $96^\circ$ , anterior limb 11 cm. and posterior limb 7 cm. long. As determined by mathematical calculations, in standing on one foot as above referred to, less than 50 pounds would be transmitted along the anterior limb and over 100 pounds along the posterior limb of the arch. I have placed all ligaments holding the limbs of the

<sup>4</sup>Practical Remarks on Shoes. Medical News, Aug. 14, 1897, vol. 71, p. 199.

<sup>5</sup>Flexibility of the Human Foot. Trans. Am. Orth. Assn., 1898, vol. xi, p. 426.

arch in position at one place, *i. e.*, one-third the way from the top of the arch. The strain on the ligaments in this case would be about 230 pounds. Add a heel well back on the foot so that the posterior limb is lengthened without changing the working angle of the foot, as shown in Fig. 12. By lengthening the posterior limb 4 cm. I make it equal to the anterior limb, the angle of the arch remaining the same. *CAB* is now an isosceles triangle. An equal amount of body weight is transmitted along each limb, namely 75 pounds, an increase of over 30 pounds on the anterior limb, which we know is not as well adapted to continuous weight-bearing as the posterior limb. The strain on the ligament has been increased from about 230 pounds to about 250 pounds. When the two limbs are equal there is the greatest amount of strain possible on the ligaments for an arch of that angle bearing that weight. By increasing the height of the heel so that the posterior limb will be longer than the anterior, more weight will be transmitted down the anterior than the posterior limb, but the strain on the ligaments will be less than when the two limbs were of the same length. In nearly all shoes, specially very high-heeled ones, the heel is placed forward so that it does not form a direct continuation of the posterior limb but is anterior to it, as shown in Fig. 13. In such shoes the actual working angle of the arch is lessened, for the heel, acting as a prop to the arch, is more in line with the transmission of the body weight than the posterior limb. Therefore, the strain on the ligaments of the arch is less than when the heel is a direct prolongation of the posterior limb. As in the other instance, the strain on each limb of the arch is in inverse proportion to its length, the greater amount being transmitted down the shorter limb. As shown in Figs. 12 and 13 by the angle *EBF*, and also in Fig 14, the heel has the same effect as the "spring" in the shoe, holding the toes in a position of dorsal flexion, thus lowering the transverse arch.

To summarize, we may say in favor of a heel:

1. If placed forward on the shoe the working angle of the arch is diminished, thus there is less strain on the ligaments maintaining the arch (see Fig. 13).
2. The body weight being thrown forward, walking is a little easier, less muscular effort being required.
3. It helps to prevent slipping. This is noticeable especially in walking down hill.
4. By elevating the posterior limb, the actual working lever of the foot becomes a little longer.
5. We are accustomed to heels, they are fashionable and make the wearer appear taller.

Against a heel may be said:

1. It creates a deformity which acts not only as such, but also changes the arches so that there is a redistribution of work to be done, and work falls on parts ill adapted to perform it.
2. There is an increase in the amount of strain on the anterior portion of the foot, which is not as well adapted to receiving it as the posterior (see Figs. 12 and 13).
3. The function of the transverse arch is interfered with

or lost by the toes being maintained in dorsal flexion (see Figs. 12, 13 and 14).

4. Heels are usually unstable, the instability increasing with the height, smallness of their diameter and forward position on the shoe.

5. The front of the foot is forced into the toe of the shoe.

6. The strain on the ligaments maintaining the arch is increased unless the heel is placed forward—the further forward the heel the less the strain, but with greater injury to the rest of the foot. Should the heel be placed so far forward that it would be directly in line with the transmission of the body weight to the ground, there would be very little strain on the ligaments, and it would be as though we were walking on stilts, in other words, as though our foot had been replaced by a wooden stump.

#### THE EFFECT OF BED-CLOTHES.

Since we spend about one-third of our lives in bed, the effect of the weight of the bed-clothes on the feet may well be considered. During sleep our muscles are relaxed and the strain falls on the ligaments and the bony structures, and none of it is supported by the muscles as it is to a greater or less extent in walking and standing. While sleeping on our back the weight of the bed-clothes falls on the inner side of the big toe, causing hallux valgus and abduction of the foot. In lying on either side one foot is supported in the abducted and the other in the adducted position. In the prone position the force is in the direction of hallux valgus and abduction. It would seem advisable that cradles, such as are used in the treatment of fractures to remove the weight of the bed-clothes from the feet, should be more generally used in cases of prolonged illness. For a foot weakened by the ill health of the patient would the more readily be influenced by forces causing abduction and hallux valgus.

#### PROPER FOOT WEAR.

Since birth forces, some great, others small, have been brought to bear on our feet, interfering with the position of greatest strength and aiding that of weakness. The stocking supplements the work of the shoe and the bed-clothes at night maintain the results of both, so that hallux valgus and the weakened foot are only too common. The question arises, what may we as physicians do to prevent this? Some have suggested placing a pad of leather under the long arch of the foot of infants in whom the pad of fat is lacking, until the foot become stronger. We should see that children wear right and left stockings with straight inner edges, which do not help to cause hallux valgus.

The shoes of infants should be distinctly right and left. The front of the shoe should be adducted, the inner edge straight, and there should be room along the straight inner edge for the front of the foot and the big toe to assume their positions of greatest strength. People so brought up would undoubtedly exercise more and what would be

prophylaxis, for the foot would be prophylaxis for the rest of the body.

As for adults, they too should wear right and left stockings and, better, with a separate apartment for the big toe. Right and left stocking can be purchased at about the same price as other stockings, and an apartment for the big toe can readily be made by placing a piece of wood the size of the big toe in the stocking and slitting the toe of the stocking down as far as the length of the toe indicated by a notch in the wood. If we now sew up the sides of the slit we have a mitten stocking.

The shoe for a normal foot or one nearly so, which can voluntarily assume the positions of strength, should have the following features:

1. Most important of all is that the angle of lateral deflection of the shoe be the same as that of the foot in its adducted position, as shown in Figs. 4, 5, 20 and 21.

2. A straight inner edge or, if hallux valgus exists, an inner edge a little straighter than the inner edge of the foot, thereby better supporting the long arch and preventing pronation.

3. The front of the shoe of the same depth along the inner edge as the thickness of the foot at that place, thus permitting the thickest portion of the front of the foot, the big toe and inner side to assume their proper positions, as shown in Figs. 4 and 5. An incorrect form is shown in Fig. 6.

4. The shoe convex, not concave, along the outer border of the shank at the mediotarsal articulation. If convex we have pressure at this point, interfering with adduction, shown in Figs. 4 and 5. An incorrect form is shown in Fig. 8.

5. The forward part of the shoe should be as wide as the weight-bearing portion of the foot at that point and room for the individual toes to rest on the sole.

6. The posterior portion of the shoe should grasp the heel of the foot *firmly* and be well supported. The stiffening should not extend beyond the mediotarsal joint.

7. There should be no spring, *i.e.* dorsal flexion of the front of the shoe which interferes with walking and lessens or destroys the transverse arch.

8. The distance from points in the shoe corresponding to the heel and distal end of the first metatarsal bone must be the same as in the foot. If the distance in the shoe is longer, adduction is interfered with, as shown in Fig. 7.

9. The shank of the sole should be convex along the outer border, thus better supporting the outer arch of the foot; it should also be higher on the inner edge and not so wide but that the upper of the shoe can snugly fit the instep.

10. The sole of the front of the shoe should be flat from side to side.

11. The lower and broader the heel the better.

12. A steel spring in the shank of the shoe helps maintain the shape of the shoe and thus that of the foot.

13. A little Scotch or lateral extension of the sole makes our base of support wider, renders the parallel gait easier

and if broader along the inner side than the outer it hinders pronation.

14. The bottom of the last or the inner sole pattern must include the area covered by the weight-bearing portion of the foot, as shown in Fig. 20.

There can be purchased many so-called reform shoes, but usually there are one or more features preventing the foot from assuming the adducted position in the shoe, as shown in Figs. 6, 7 and 8.



FIG. 15. Shows the relation of an incorrect to a correct last. The dotted lines indicate the original form of the front of the last.

Even though the form of the shoe be correct, should the angle of lateral deflection of the shoe be less than that of the foot, the foot would not be able to assume the adducted position. On the other hand, if the angle of lateral deflection of the shoe is more than that of the foot, the shoe will be exceedingly uncomfortable, because of pressure on the small toes and outer side of the foot (see Fig. 21). It is as much of a physiological impossibility to wear ready-made shoes as ready-made false teeth, the only difference being

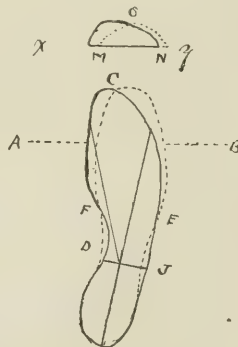


FIG. 16. Shows the bottom of an incorrect last represented by the dotted lines altered to fit a foot in which when adducted the angle of lateral deflection is equal to 22°. CAF and m x o show the amount it has been necessary to build out the last along the inner edge. CBE and NOy the amount cut away from the outer edge. The last has been built out at J so that the foot may assume the adducted position, and cut away at D which will lift up the arch and favor adduction. x y represents a cross section of the two lasts at A B, the adducted last highest in the middle has been changed to an adducted last, deepest along the inner edge.

that the alveolar process cannot adapt itself to the plate, while the foot can in a measure adapt itself to the ready-made shoe, but only under pathological conditions. It would be difficult to find two feet of the same length and width, in

which the distance from the heel to the distal end of the first metatarsal is the same, and the same thickness along the inner portion of the front of the foot and still most important of all, the same angle of lateral deflection when the foot is adducted. For this angle may vary from 15 to 35 degrees. The shoe for one foot would not fit the other under physiological conditions (see Fig. 21). It would seem that those of us who wish to wear proper shoes must have our shoes made over a last constructed for our feet. Two

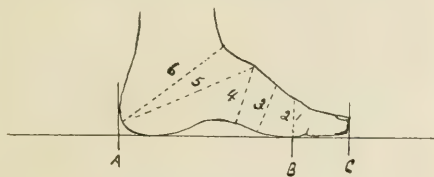


FIG. 17. Shows tracing of the inner side of the foot with lines indicating where measurements are to be taken. Place a piece of glass 10 x 12 inches or larger, on the side of the foot, and with pen and ink or wax pencil, trace the foot on the glass. Transfer the outline to paper by placing a piece of paper on the glass, holding them up to the light and following the lines with a pencil. AB = length from heel to distal end of first metatarsal bone, (7). AC = length of foot, (8).

last manufacturers have made lasts for me which have proven fairly satisfactory. I send them the following outlines and measurements:

1. Mark the foot with skin pencil or ink as indicated in Fig. 17. Place a plate of glass 10 x 12 inches on the inner side of the foot and trace on it with ink or a wax pencil the outline of the foot, including the lines indicating where measurements are to be made. The tracing on the glass can readily be transferred to paper by laying a piece of white

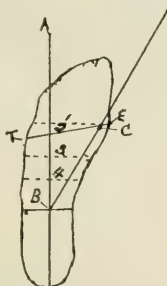


FIG. 18. Shows tracing of sole of foot in adducted position, made by marking around the foot with a pencil, flat on one side, held perpendicular except under long arch. ABC = angle of lateral deflection. 1, 2, 3 and 4 lines where 1, 2, 3, 4 of Fig. 17 cross the foot. TE position of the transverse arch.

paper over it and holding it up to the light and following the lines with a pencil. Make the eight measurements indicated. This outline shows just where the measurements were taken and at the same time furnishes an idea of the shape of the foot, and gives length of the shank and entire foot.

2. Make an outline of the sole of the foot voluntarily adducted on paper by means of a pencil held perpendicular and drawn around the foot, and on this outline draw the angle of lateral deflection, position of the transverse arch,

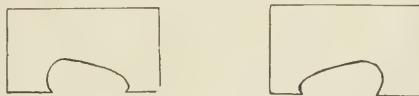


FIG. 19. Card board pattern of cross section of the foot through the transverse arch. Made by folding a lead tape over the front of the foot at TE, Fig. 18, then lay the tape on edge and cut out the pattern. Last must conform to this pattern at this place.

and mark lines indicating where the lines of measurement cross the bottom of the foot (see Fig. 18).

3. Mould a piece of sheet lead 1 cm. wide, and about 2 mm. thick, over the front of the foot from the distal end of



FIG. 20. Shaded area represents an impression of the foot on smoked paper, i. e., the weight bearing portion of the foot. The dotted line represents an outline of the foot made by drawing a pencil, flattened on one side and held perpendicular, around the foot. The inner sole pattern for the shoe, i. e., the bottom of the last, must include the area covered by the weight bearing portion of the foot and is outlined by the solid line.

the first metatarsal bone to the distal end of the fifth bone. This is lifted from the foot, placed on edge on paper and the lower surface outlined with a pencil. This forms an outline of a cross section of the foot at this place, namely,

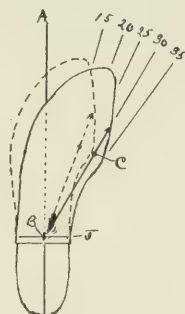


FIG. 21. Card board model showing the changes in shape of an inner sole pattern of a last from 15° to 35°. An inner sole pattern is cut out of card board, then cut in two and fastened on a background of card board, by means of a McGill fastener, through the centre of the mediotalar point J. The line BC is drawn on the inner sole pattern, and the angles of 15° to 35° are drawn on the background. The inner sole pattern will have an angle of lateral deflection from 15°-35° according to the number to which BC points. One sees the difference in form of one of 20° and 30°, and how a shoe of 20° would not fit a foot of 30°, and vice versa.

through the transverse arch (see Fig. 19). The last must correspond to this pattern at this place. Both these manufacturers have a model of a proper last which I furnished them.

Lasts are made by them, having the form of this model, but differing from it according to the measurements and outlines given. After receiving the lasts have a custom shoemaker measure the feet and the lasts and make what changes are necessary to have the shoes fit the feet. Changes should be made in size and not in form.

A cheap way to see whether one's last is correct or not is to cut out an inner sole of card-board, fasten it on the last with a roller gauze bandage. Now wind a wet crinoline bandage over this; set aside to dry; when dry slit down the centre of the front as in a lace shoe, remove the last and try on the crinoline shoe, then alter as seems necessary.

Shoes can be made from one's last either by a custom shoemaker, or if one desires cheaper shoes, at any of the large manufacturers who have stores in our cities; in the latter places shoes costing from three to five dollars ready-made can be obtained, made on your last, for four to six dollars. My idea in describing the above in detail is to show how feasible it is to wear proper foot gear, the only trouble being to start with the proper last. A little painstaking at the onset will insure much comfort afterwards at a very little increase in price.

#### THE WEAKENED FOOT.

We are all acquainted with that form of the weakened foot known as the abducted or pronated foot. The two movements go together, viz. abduction and rolling over inwards or pronation. The gait of such an individual is clumsy and heavy, the internal malleolus is very prominent, and the ability to voluntarily adduct the foot is lessened or lost. The symptoms vary, being weak ankles, tired feet, pain in the calf, etc. There is an actual lowering of the long arch and the line between the pronated and flat foot is an arbitrary one. What may we do for such a foot? If we ask a person with pronated feet to stand and we hold his feet in the adducted position, we notice that the long arch is supported and pronation is prevented and the body weight no longer falls to the inner side of the long arch, but over the outer border of the foot which, as we know, is better adapted to receiving it. To treat the weakened foot, first have a shoe made as one would for the normal foot, but differing from it as follows: The angle of lateral deflection of the shoe must equal that of the foot when held in the adducted position as just described. Increase the forces causing adduction by filing away the last at points corresponding to 1, 2 and 3 of Fig. 1. This will cause the shoe to make pressure at these points. The heel and sole should project out further from the shoe on the inner side than the outer. This will interfere with the rolling over inwards or pronation. Before having the shoes made, fasten an inner sole of leather 2 mm. thick on the bottom of the last to make room for an inner sole which

is to be worn in the shoe. Better have lace shoes and lacing to extend well down to the tip, as in the bicycle pattern, then the foot can more readily slip in the shoe fitted with devices about to be described, than in the usual form of shoe. From our knowledge of the abducted foot we know that it is

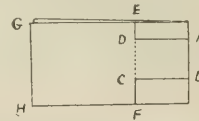


FIG. 22. Making the pattern for a toe post. A heavy piece of paper folded once along the line AB. ADE and BCF are cut away, leaving the tongue ADCB. AD should equal the depth of the shoe at that point, and AB should be as wide as the length of the slit in the card board inner sole. The tongue is inserted in the slit, and the bases folded back and cut away to conform to the front of the inner sole. When removed and straightened out this forms the pattern in Fig. 23.

unable to assume or maintain without assistance in the shoe the position of strength, namely, adduction. To hold the foot in the shoe in this position we must either cause pressure on the outer side of the front of the foot, thus cramping the toes and making the feet very uncomfortable, or else use

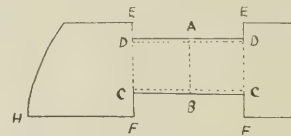


FIG. 23. Pattern of paper from which the tin is cut. The edges DD and CC are to be turned in. Tin is folded along the dotted lines AB—DC and DC forming the toe post in Fig. 24.

some other means. For nearly one year I have been wearing a device for holding the foot in the adducted position, which, with the aid of proper foot gear has relieved me from all the previous disagreeable symptoms. The device may be called a toe-post. It is represented in Fig. 24. It is main-



FIG. 24. Shows the toe post ready to be inserted into the card board inner sole. Rough points on the upper and under surfaces of the base, which are made by punching holes with an awl, hold the toe post to both the inner sole of the shoe and the card board inner sole.

tained in its proper position in the shoe by means of an inner sole with a slit between the positions of the large and second toe, through which the upright of the toe-post projects (see Fig. 28). To make a toe-post:

First cut an inner sole of card-board 1.5 to 2 mm. thick, having the outlines of the sole of the last, for it must exactly fit the inside of the shoe. Place the foot on this inner

sole held in the adducted position, the big toe held along the inner edge and with a pencil mark a line between the big and second toe. Remove a small slip of card-board 2 cm. long and 3 mm. wide along this line, leaving a slit in the inner sole. The posterior end of the slit should be about 1.5 cm. anterior to the front of the foot between the two toes. To make a pattern for the toe-post follow the directions in Figs. 22 and 23. With heavy shears cut out from tin according to the pattern, using No. IC or IX tin. The tin is to be folded as indicated in Fig. 23. The folding should be rounded, not angular, thus imparting elasticity to the toe-post. Slip the upright portion of the toe-post through the slit in the card-board inner sole and trim the edges of the bases if necessary, so that they will not project beyond the edge of the card-board inner sole. Place

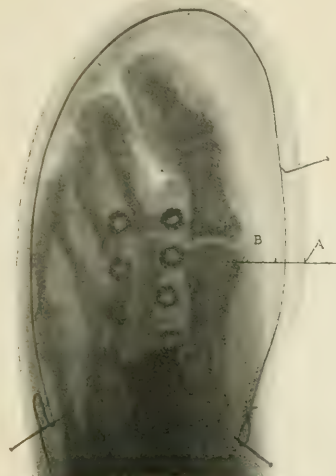


FIG. 25. A skiagraph of a weakened foot having an angle of lateral deflection of  $18^\circ$  in a shoe whose angle of lateral deflection is  $25^\circ$ . Hallux valgus is present. The inner portion of the shoe is not occupied by the front of the foot A, the inner edge of the sole is 22 mm. from B, the inner edge of the 1st metatarsal bone. The outer edge of the foot after "breaking in" the shoe would overhang the outer edge of the sole.

it in the shoe and try it. If any adjusting is necessary, change the position of the slit in the inner sole as needed. Make sure that the post does not strike the front of the foot. I prefer a card-board to a leather inner sole, because the card-board, by absorbing moisture, keeps the feet dry. New inner soles should be used every week. One has a feeling of satisfaction in throwing away a certain amount of filth and perspiration which would otherwise have been retained in the shoes. After having determined the proper position for the slit keep an inner sole as a model from which to make others. The patterns for one foot reversed serve as patterns for the other. It is not any more trouble to change the card-board inner soles than to change one's stockings,

and the hygienic reasons for both are the same. For indeed all phases of civilization are comparative, and individuals who bathe once a day and those who bathe once a week may both be classed as civilized and living under hygienic conditions.

To illustrate the effects of the toe-post, I have taken skiagraphs of the foot within a shoe. Fig. 25 shows the foot in the shoe without the toe-post. In Fig. 26 the foot is adducted and hallux valgus has been overcome by the toe-post. The line about the foot is caused by a wire placed in the crease between the upper and the sole in order to more clearly outline the shoe.

I have worn the toe-post for a year under all conditions, as tramping, tennis, golf, in the operating room, etc. I have worn it in one shoe one day and in the other shoe the

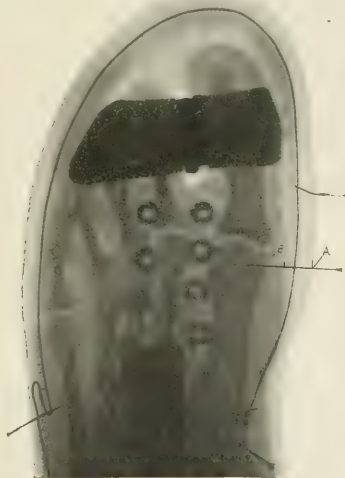


FIG. 26. A skiagraph which shows the same foot and shoe taken with a toe post, otherwise under similar conditions as in Fig. 25. The foot is held in the adducted position and has the mechanical advantages of a foot with an angle of lateral deflection equal to  $25^\circ$ . The inner portion of the shoe is occupied by the front of the foot. A B = 16 mm. instead of 22 mm. as in Fig. 25. The hallux valgus has been corrected. The outer edge of the foot will not overhang the outer edge of the sole.

next and at the end of the day the foot supported by the toe-post would feel strong while the other would be tired. The toe-post maintains the foot in the adducted position, prevents hallux valgus, and does not cause discomfort when properly adjusted. There is a greater sense of security for the shoe seems to be a part of the foot and the foot grasps the shoe in walking. The Greeks wore sandals with a leather thong between the first and second toe, holding the sandal in position. Judging from their statues they did not suffer from pronated feet and we have never heard of their shoes hurting them. The principle is the same in the toe-post.

In favor of a toe-post such as I describe I think it may be said:

1. That the weakened foot which can be passively adducted—with the toe-post and the aid of a proper shoe—may be relieved from its previous symptoms, for it holds the foot in the adducted position, thus naturally supporting the long arch, prevents the rolling over inwards and overcomes hallux valgus.

2. That it is not only comfortable, but gives one a greater sense of security and strength.



FIG. 27. Shows foot adductor made of heavy tin and fitted over the last at a place corresponding to the middle  $\frac{3}{4}$  of the fifth metatarsal bone. This slips over the card board inner sole as shown in Fig. 28. It also has rough points to prevent displacement as in the toe post.

3. It is simple, easily made and, fitting in a slit in an inner sole, any adjustment necessary can readily be done which would be impossible if it was incorporated in the structure of the shoe.

Another means of holding the foot in the adducted position is represented in Fig. 27. It helps out the toe-post and is comfortable. It can be made from XX tin. Fig. 28 shows a card-board inner sole with toe-post and foot adductor in position.

While sleeping, nearly the entire human mechanism is at rest. As I have pointed out, no matter what position we may assume, strain falls on the structure of one or both feet

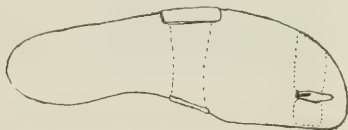


FIG. 28. Card board inner sole with toe post and foot adductor attached.

in such a manner as to cause hallux valgus and abduction. It is obvious if we wish more than temporary relief that our feet must be treated by night as well as by day. For two years I have worn at night a big toe and foot adductor. This device is not uncomfortable, it overcomes hallux valgus, maintains the foot in the adducted position, thus relieving ligaments which have been stretched during the day. There are other means of treating the pronated foot, as massage, forcible adduction of the foot and gymnastics. These are all important adjuncts to whatever mechanical means we may employ. In extreme cases a flat foot brace, if it can be worn, is of great service, for when we elevate the arch we adduct the foot and pronation is interfered with. One thing more about the treatment of

the weakened foot. Do not simply relieve symptoms but let the treatment be progressive and when new shoes are necessary see if the foot will not stand a little more adduction and alter your lasts as necessary. At present I am able to wear a shoe which would have been impossible a year ago. In altering a last to increase the adducted position cut away the last at places 1, 2, 3 of Fig. 1; thus we increase the adducting forces. This causes the shoe to make pressure at the mediotarsal joint on the inner side of the foot and counter-pressure at the heel below the mediotarsal joint and



FIG. 29. Foot and big toe adductor to be worn at night. It consists of a curved piece of wood, W with a leather loop, L which fits over the big toe. When the thongs are tied as represented in Fig. 29, the foot and the big toe are adducted.

over the fifth metatarsal bone on the outer side. The foot will now become more adducted if there is room. This is furnished by adding leather to the last at places 1, 2, 3, Fig. 2. This diminishes the abducting forces and permits the foot to assume the adducted position.

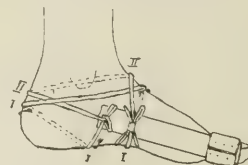


FIG. 30. Foot and big toe adductor as applied to the foot.

#### FLAT FOOT.

Two of the most noticeable features of the flattened foot are the lowering of the arch and abduction. We have considered the effect of the abducted position. Now let us consider what effect the lowering of the arch has upon the structure and mechanism of the foot. The transition from a normal and weakened foot to a flattened foot is so gradual that it is hard to say just where to draw the line. In considering the transmission of the body weight through the foot to the ground and for the sake of obtaining some idea of the strain on the ligaments of the arch and the relative

amount of weight transmitted down each limb, I resolved the anterior limbs of the tripod into one and considered what would be the effect on the ligaments and limbs of the long arch.

The following table based on mathematical calculations gives some idea of what effect the lowering of the long arch would have on the ligaments of the arch and the relative amount of the body weight transmitted down each limb, the individual weighing 150 pounds, standing on one foot, in the erect posture and the weight falling over the long arch.

The effect of lowering the arch of the foot, individual weighing 150 pounds, erect posture, entire weight on one foot:

Angle of the arch..	96°	116°	124°	150°	160°	170°	179°-30'	180°
Amount weight trans-								
mitted down ant. limb	44	47	60	65	68	71	74 +	0
Amount weight trans-								
mitted post. limb	106	103	90	85	82	79	76 (about)	0
Strain on ligaments placed $\frac{1}{2}$ way top arch	228	342	413	833	1263	2308	17,475	0

From the study of the above table we see that as the arch becomes lower and the angle greater, more of the body weight is transmitted down the anterior limb of the arch, which is ill-adapted to receiving it, and most important of all, the strain on the ligaments becomes greater, an increase from less than 300 pounds in the normal foot to several thousand in the marked flat foot. When the arch has been completely destroyed both the anterior and posterior limbs and ligaments are relieved from any strain in the transmission of the body weight, for the entire weight is transmitted directly to the ground through the bottom of the foot. The most important factor in the treatment of flat foot is that of prophylaxis. One cannot begin too early, for it is much easier to correct an arch whose ligaments have been under a strain of a few hundred pounds than one which has been under a strain of several thousand pounds. We may classify flat feet into the mobile, those which can be passively adducted and the arch increased, and the rigid form. Do not treat the rigid flat foot with a brace until the deformity has been passively corrected, for the surgeon who fits a brace to a rigid flat foot is in the same position as the gynecologist who treats an adherent retroflexed uterus with a pessary. In both cases the mechanical supports will injure soft parts and not do any good. Two features in flat foot must be corrected; first, the lowering of the arch, and second, the abduction of the foot. When we correct one we aid the other, but when we treat both our results will be four-fold. Begin with proper shoes which maintain the foot in the adducted position, as for the pronated feet. How often the surgeon has his patient wear a flat-foot brace, a brace which elevates the arch and thereby tends to adduct the foot, in a shoe in which adduction is interfered with or impossible. In these the additional support afforded to the arch by adduction of the foot is lost and the elevation of the arch is interfered with, because its associated movement adduction

is impossible. After obtaining proper shoes, have a brace made which will accurately fit the foot and not only support the arch but maintain the foot in the adducted position.

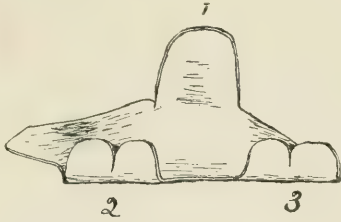


FIG. 31. Plate for flat foot, made from No. 20 sheet steel. It supports the arch, thereby adducting the foot, and by holding the foot in the adducted position by forces 1, 2 and 3, the arch is maintained. The view is from the outer side. 1 is the flange on the inner side fitting over the astragalo-scapoid articulation. 2 represents the anterior flange fitting over the middle  $\frac{2}{3}$  of the fifth metatarsal bone. 3 is the posterior flange fitting over the os calcis posterior to the mediatarsal joint.

A brace for flat feet which I have worn and found very comfortable is shown in Figs. 31, 32, 33 and 34. This brace supports the arch, thereby also adducting the foot

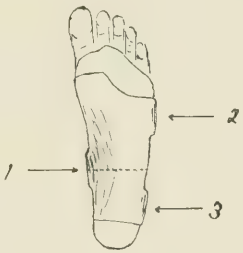


FIG. 32. Flat foot brace applied to the foot. The foot is held in the adducted position by the flanges as indicated, which act as the adducting forces 1, 2 and 3.

and vice versa; the arch also supports the adducted position. If one wishes to hold a foot in the adducted position it can be done most readily by grasping the foot with two



FIG. 33.

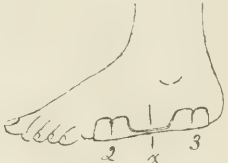


FIG. 34.

FIG. 33. Inner view of flat foot brace. Inner flange 1, fits over the astragalo-scapoid articulation, thus preventing the rolling over inwards of the foot, and with the two outer flanges it holds the foot in the adducted position.

FIG. 34. Outer view of flat foot brace showing the flanges 2 and 3 which, with 1, hold the foot in the adducted position. There is no pressure over the calcano-cuboid joint at x which would cause abduction.

hands, the two thumbs being close together, and making pressure against the astragalo-scapoid articulation and the fingers of one hand grasping the front of the foot over the fifth metatarsal bone and the fingers of the other hand grasping the heel. These forces we may resolve into the adducting forces 1, 2 and 3 as represented in Fig 1, etc. This brace employs the same forces: flange 1 makes pressure over the astragalo-scapoid articulation and prevents the rolling over inward of the weakened foot. As the long arch is elevated more of the body weight falls to the outer side of the foot. The body weight and inner flange 1 are resisted by the two outer flanges, 2, fitting over the middle two-thirds of the fifth metatarsal bone and 3 over the heel posterior to the mediotarsal articulation; thus the foot is held in the adducted position. It would seem that any brace which has a flange fitting over the calcaneo-cuboid articulation on the outer side of the foot must abduct the foot, thus interfering with the elevation of the arch. When the long inner arch is elevated and more weight is thrown to the outer arch of the foot, this weight will be opposed by this flange, which will act as the abducting force 1, and the body weight as abducting force 2 and 3 (see Fig. 2). These are the same forces one would use to straighten a bent stick. We would grasp the stick with both hands and the opposing force, as our knee, would be placed against the angle in the stick. Thus such a brace must straighten, *i. e.* abduct the foot and thereby interfere with its own action. It is essential that a brace such as I have described shall fit the foot accurately, otherwise it will be very uncomfortable or else not do any good.

#### TO MAKE A FLAT-FOOT BRACE.

First make plaster casts of the feet in the adducted position. To do this have the patient sit in a chair with the leg of the foot from which the cast is to be taken resting on the knee of the other leg. Having poured enough plaster on a piece of paper on another chair near enough for the foot to rest on, let the foot sink into the plaster with the outer side of the foot down and the long axis of the foot horizontal. As it sinks adduct the foot by lifting up the big toe and hold it adducted until the plaster has hardened. Rub some vaseline over the edges of the plaster and a little over the foot and cover the rest of the foot with plaster. When the plaster has hardened separate the two halves, re-vaseline and tie together and this will form the mold for the cast. After making the cast, mark the mediotarsal joint and the tuberosity of the fifth metatarsal bone. Outline the brace as shown in Figs. 31, 32, 33 and 34. The casts may need a little trimming, the arch may be increased a little. From these casts the braces are made according to the outline, using No. 20 or 22 sheet steel. These braces assume their proper positions in the proper shoe and do what is claimed for them. A toe-post also helps out the flat-foot brace by overcoming the hallux valgus and helps in maintaining the adducted position.

If I have written anything of practical value in this article, special thanks are due to my own feet, which without grumbling have stood all kinds of experiments and have constantly been urging me during the last three years that something must be done for bettering the foot and its covering both in its normal and weakened conditions.

## MASTITIS IN TYPHOID FEVER, WITH THE REPORT OF THREE CASES.

BY THOMAS MCCRAE, M. B.,

*Associate in Medicine, The Johns Hopkins University, and  
Resident Physician, The Johns Hopkins Hospital.*

Mastitis is apparently one of the rarest glandular complications of typhoid fever, and occurs much less frequently than orchitis, thyroiditis or parotitis. The cases here reported are the first in over one thousand cases of typhoid fever in the Johns Hopkins Hospital. That the first two should have been in the wards at the same time is another example of the coincidence of rare conditions.

In the literature but few references to this complication were found. The text-books of medicine, so far as discovered, do not mention it. Keen and Hare in their monographs on the surgical and medical complications of typhoid fever do not refer to it, nor do the majority of articles even allude to it. There has been much written on the occurrence of suppuration in typhoid fever, but rarely is any note made of abscess formation in the breast. No reference to this condition was found in any of the works on diseases of

the breast which were consulted. Hölscher (1), Sorel (2), and Scheele (3) in giving the post-mortem findings of 3171 cases of typhoid fever do not report a single instance.

Berg (4) in reporting the statistics of 1626 cases of typhoid fever found mastitis in four instances, but no clinical account is given of them. Curschmann in his work on typhoid fever in Nothnagel's system alludes to the rarity of the condition, although a slight degree of swelling of the breast is, in his opinion, not uncommon. He mentions having seen two instances of mastitis in young men. Vallin (5), in the report of a discussion on orchitis and parotitis in typhoid fever, mentions having had one case of mastitis, but gives no clinical account. An interesting series of cases is reported by Leudet (6), who saw five in a period of about ten years. His patients were all females, aged from 21 to 28 years, and only one of them had nursed a child. The

mastitis occurred in the third or fourth week and involved both breasts in two of the cases. In none did suppuration occur, nor did the complication have any unfavorable influence on the course of the disease. In three of his patients hæmorrhage occurred, in two from the uterus and in one from the nose, the last so profuse that plugging was necessary. Leudet very naturally drew the conclusion that mastitis was frequently associated with hæmorrhages, and these especially from the uterus. Destree (7) reports two instances. They were in males, aged 26 and 27 years. The mastitis occurred at the end of the third week, suppuration followed in both and staphylococci were found.

Charlotte West (8), in the report of a case with unusual complications in a girl of seventeen, states that at the beginning of the third week swelling and tenderness developed in both breasts. These subsided and in the fourth week thrombophlebitis was found in both legs, both arms and both breasts. Suppuration followed in one leg, one arm and both breasts. Saline infusions had been given into the breasts, but the writer does not think they were associated with the suppuration. Fornaca (9), in reporting a case draws attention to its rarity. His patient was a woman, aged 40 years. On the 29th day of the disease, after convalescence had begun, mastitis appeared in the right breast. With this there was a relapse accompanied by fever lasting for twelve days. On the fifth day after the swelling appeared a puncture was made into it and sero-purulent fluid obtained. Cultures from this showed the presence of the bacillus of Eberth. The bacilli in the culture agglutinated with the patient's serum. On the seventeenth day of the relapse the left breast was also affected, and a week later there was a third period of fever, lasting for four days. On the seventy-fourth day after admission the right breast was almost at its normal size, but the left was still enlarged and indurated.

Cappellari (10) reports another instance of mastitis with suppuration. His patient was a girl, aged fifteen years, who in the fourth week had swelling of the left breast. This increased, became hard and the temperature, which had returned to normal, became elevated. Fluctuation finally was felt, the abscess was opened and recovery followed. There is no note regarding cultures. The nipple was not affected, nor the axillary glands of that side. Davis, Patterson and Hewlett (11) report an interesting case from the New York Hospital. Their patient was a woman, aged 34 years, who went through a moderately severe attack, the temperature touching normal on the 36th day. Three days later she began to complain of pain in the left breast, which, on the 41st day, was swollen. On the next day the right breast became tender. The swelling and tenderness of the left breast increased, and on the 51st day fluctuation was detected and pus obtained on aspiration. The temperature had become elevated, reaching over 103° in the afternoon and falling to normal in the morning. The leucocytes on the 49th day were 13,200. On the 52d day the abscess was freely opened and 150 cc. of pus obtained. Recovery was without incident. The induration in the right breast

gradually diminished. The cultures from the pus showed typhoid bacilli.

The histories of the three cases to be reported are given below. Suppuration occurred in two. They were all in the service of Professor Osler.

*CASE 1.—Severe attack of typhoid fever; mastitis on the 30th day; suppuration; incision; recovery.*

M. W., colored, female, married, aged 27, was admitted on July 19, 1900, on the 14th day of her illness. She had three children, the oldest nine and the youngest five years old. In the two years before admission she had two miscarriages. There was nothing unusual in the history of her illness. On admission her general condition was good; she had rose spots and an enlarged spleen. The Widal reaction was given the day after admission. The leucocytes were 4000 per cmm. The attack was severe, but there was nothing of special note until the 29th day, when the first signs of breast trouble were noted. The temperature for a week before had not been above 102°, and averaged from 100° to 101°. On August 4, the 30th day of the disease, it was noted that in the upper outer quadrant of the left breast there was an indurated mass the size of a hen's egg. This was painful and very tender. There was slight visible prominence over it but no redness. On August 7 the swelling had increased. There was marked tenderness and a slight feeling of fluctuation. The leucocytes were 8000 per cmm. On the following day there was marked redness, and in the evening the temperature rose to 104°. On August 9, the 35th day, the breast was opened in the left upper quadrant and a considerable amount of pus obtained. The temperature, which had been 99.3° in the morning, rose to 104° at noon. On the next day an incision was made in the left lower quadrant, but no pus was found. After this the temperature soon fell, reaching normal on the 46th day. The subsequent course was uneventful. The discharge from the breast rapidly diminished and the wound was healed by August 22, the 48th day.

In this case, which was moderately severe in character, no special change in the course was caused by the occurrence of mastitis. The pain in the breast and the two elevations of temperature to 104° without any chill were the principal features. The absence of a pronounced leucocytosis is to be noted. It is to be regretted that no cultures were obtained from the pus.

*CASE 2.—Moderate attack of typhoid fever; mastitis in right breast on 13th day; in left breast on 18th day; relapse; second attack of mastitis in the left breast on 52d day; recovery.*

M. B., white, female, married, aged 25, was admitted on July 25, 1900, on the fifth day of the disease. She had one child, 18 months old, that she had nursed for 10 months. On admission there were rose spots, an enlarged spleen and a positive Widal reaction. From admission until August 1 there were no special features. The temperature ranged from 102° to 103°. The leucocytes varied from 3300 to 3500 per cmm. On August 2, the 13th day of the disease, the patient complained of severe pain in the right breast,

and on palpation a small area of induration was made out in the upper right quadrant. This was very painful. There was no redness over it. The leucocytes were 8000 per cmm. On the following day the condition of the breast was unchanged. The leucocytes were 10,000 per cmm. On August 4, the induration was less marked and there was less pain. The leucocytes were 8000 per cmm. On August 5 the induration had almost disappeared and the leucocytes were 5500 per cmm. On August 7, complaint was made of pain in the left breast and practically the same condition was found. This also disappeared after a few days. In neither breast was there any suppuration. The temperature had apparently not been influenced, and by August 9, the 20th day, had fallen nearly to normal. After this it gradually rose and continued elevated for nearly three weeks, the patient having a typical relapse with fresh rose spots. Recovery was slow and the temperature had not reached normal when, on September 10—the 52d day—she complained of pain in the left breast. An area of induration was found in the upper outer quadrant about the size of a hen's egg. There was marked tenderness. The skin over it was not inflamed, nor was there any sense of fluctuation. The glands in the left axilla were not enlarged. The temperature was about 101°. The leucocytes were 18,000 per cmm. On September 12, the temperature rose to 103° without any chill, but fell on the next day and the swelling rapidly diminished. After this the temperature was normal, recovery was rapid, and she was discharged perfectly well on September 24, the 66th day. Both breasts were quite normal, and subsequently she said there had not been any symptoms from them.

The point of special interest in this case is the occurrence of mastitis without suppuration three times during the attack of typhoid fever. Beyond the pain and discomfort given to the patient, it had apparently no influence on the course of the disease. The left breast seemed perfectly normal between the two attacks. The leucocytosis is to be noted.

CASE 3.—*Moderate attack of typhoid fever; during convalescence abscess in right breast; opened; rapid recovery.*

L. L., white, female, married, aged 32 years, was admitted on September 5, 1901, on the 15th day of the disease. Her child, aged 20 months, was admitted with her. She had nursed him up to the day of admission. As he had a temperature of 103° and diarrhoea, it was at first thought that he also had typhoid fever, but the subsequent course was that of a gastro-enteritis, and he improved rapidly. His blood did not give a Widal reaction. The course of the typhoid fever patient was uneventful. There was practically no secretion from the breasts, and examination of them was negative. The Widal reaction was present. Her temperature reached normal on September 17, the 26th day. On September 21, the 30th day, she complained of some pain in the right breast, and in the outer lower quadrant was found an area of swelling with redness of the skin over it. On the following day fluctuation was made out. There was no tenderness elsewhere and the left breast was negative. The

leucocytes were 8000 per cmm. The abscess was opened and about 40 cc. of pus obtained. Cultures from this showed staphylococcus albus but no typhoid bacilli. There was no disturbance of the temperature, which continued normal throughout the attack of mastitis. The further course was uneventful. The wound healed rapidly and she was discharged well on September 30, the 39th day.

In this case there was practically no influence on the condition from the complication. The temperature continued normal and there was no leucocytosis.

In considering the reported cases it is seen that among the sixteen in which the sex is mentioned, four were males. The age varied from fifteen to forty years. The occurrence in males goes to show that it is not necessarily associated with a functioning gland. Among the females there does not seem to have been any special association with previous nursing, as, with the exception of the last case here reported, none had nursed children except at a considerable period before the attack of typhoid fever. In regard to this case, the fact that the child was admitted with fever and diarrhoea after having nursed during the first two weeks of the mother's illness, suggested a possibility of his having typhoid fever and of infection through the milk. But the subsequent course, with the absence of a Widal reaction, showed that the child did not have typhoid fever. This is an observation of interest in connection with the question as to the occurrence of typhoid bacilli in the milk of nursing women ill with typhoid fever. So far as a search of the literature has shown, there is no authentic instance of the occurrence of typhoid bacilli in the milk. There are instances of a Widal reaction being given by the blood of a nursing infant which had apparently been conveyed through the milk. This will be discussed by Dr. Lynch of this hospital in a paper shortly to be published.

Among twelve cases of which there are full reports, both breasts were involved in six instances. Suppuration occurred in seven out of fourteen cases with complete notes. It was present in both breasts in only one case. There are notes of the bacteriological findings in five cases, in one of which abscess formation did not occur, but fluid was obtained by puncture. In three staphylococci were found, and in two typhoid bacilli grew in the cultures.

As to the period of occurrence in the disease of the fourteen cases in which the data are given, it is seen that, with but one exception, it was at the end of the third week or later in the disease. The exception is the second case here reported with the first onset of mastitis on the thirteenth day. In several instances the temperature had become normal before the onset of the complication. In two patients it was associated with a relapse. The effect on the fever was very varied; in one not causing any elevation, in others causing the temperature to rise to 104°.

There are not a sufficient number of blood counts reported to draw any conclusion as to the occurrence of leucocytosis. It was present in two out of four cases. That suppuration may occur without any marked increase in the number of the

white corpuscles is shown by two of the cases here reported, in which the leucocytes were not above 8000 per cmm. This, of course, may mean a slight increase when the diminished number usually found in typhoid fever is remembered. From the second of the present cases it is evident that leucocytosis may occur without suppuration.

Lastly, in no instance did the complication appear to have any unfavorable influence on the course of the disease beyond prolonging convalescence.

#### CONCLUSIONS.

1. Mastitis is a rare complication of typhoid fever, and usually occurs late in the attack.
2. It occurs in both sexes, and is apparently not associated with a functioning gland.
3. Both breasts are involved in about half of the cases.
4. Suppuration occurs in about half of the cases and may be associated with the typhoid bacillus or staphylococcus.
5. It is of no special moment in the prognosis.

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## A PRELIMINARY REPORT ON THE BLOOD IN TWO CASES OF FILARIASIS.

By W. J. CALVERT, M.D., U. S. A.

*From the Municipal Laboratory, Board of Health, Manila, Philippine Islands.*

Examinations of the blood of Filipino prisoners of war, confined in Manila, have been made to determine, as far as possible, the prevalence of filariasis in these islands. Thus far 426 specimens have been examined, representing many districts throughout the islands. Two cases of filariasis have been found.

The blood in each of the cases shows a decided leucocytosis and a marked increase in eosinophiles. The embryos are found in varying numbers throughout the twenty-four hours.

CASE I.—A. P., native male, Filipino, born and reared in Albay; had been in Manila about two months. The previous history is vague, but as near as can be determined, the patient has had pain in the left groin and iliac region for two months. About one month since, one of the glands of the groin was somewhat enlarged and painful. Within the last month this gland has decreased in size and no further pain experienced, the physical examination being otherwise negative. The patient gives the history of indefinite attacks of fever, chills and headache. Since the patient has been under observation, one short attack of fever and chills has been noted. Eight embryos were found in one slide, taken on April 5, 1901, at 11 p. m. On April 6, 1901, at 9 a. m., one embryo was found. The embryos have the ordinary characteristics. On April 6, the blood counts showed 3,866,666 reds and 18,760 leucocytes per cmm.

#### Differential count:

Lymphocytes.....	10.66%
Polymorphonuclears.....	68.33%
Large mononuclears.....	5.66%
Transitionals.....	3.00%
Eosinophiles.....	12.33%
200 leucocytes counted.	

The highest leucocytosis found was 26,666, the lowest 18,000. The highest percentage of eosinophiles found was 22, the lowest 8. The largest number of embryos found was 1176 per cc., at 11 p. m., on April 18, 1901.

CASE II.—M. R., native male, Filipino, from Albay, was taken prisoner at the same time as case number one. The history is vague. The patient claims to have had the disease one year, during which time several attacks of fever and chills with some headache occurred. Physical examination negative, excepting a slight hydrocele on right side.

Two embryos were found in the blood taken at 11 p. m., on April 5, 1901; on April 18, 1901, the blood count showed 3,620,000 reds and 8000 whites per cmm.

#### Differential count:

Lymphocytes.....	14.00%
Polymorphonuclears.....	64.00%
Large mononuclears.....	4.50%
Transitionals.....	2.50%
Eosinophiles.....	15.00%
200 leucocytes counted.	

The highest leucocytosis found was 14,000, the lowest 7,600. The highest percentage of eosinophiles found was 20, the lowest 6. The largest number of embryos counted was 1680, at 9 p. m. on April 23, 1901.

In the first case the disease is evidently of short duration, possibly no longer than three months; while the second case is probably about a year's duration.

Frequent blood examinations, extending over a period of nearly four weeks, are rather constant.

It will be noted that the leucocytosis and the percentage of eosinophiles are higher in the first than they are in the second case. This fact, in addition to the negative findings in the blood in old cases, leads one to believe that in the early stages of filariasis, leucocytosis with an increase of the eosinophiles may be looked for, and, that as the disease progresses, the leucocytosis and increase in eosinophiles gradually decrease to normal.

## THE LAENNEC—A SOCIETY FOR THE STUDY OF TUBERCULOSIS.

In the BULLETIN for December, 1900, a brief account was given of the first meeting of The Laennec—A Society for the Study of Tuberculosis. During the past year subsequent meetings of the Society have been held regularly, and the following papers have been presented:

The Phthisiologia of Richard Morton, Prof. Osler.

Tuberculosis in the United States, Dr. Brülle.

Illustrations of Tuberculous Lesions in Literature, Dr. E. L. Opie.

Note on Tuberculous Pericarditis, Prof. Osler.

Bayle and Baillie, Dr. Fletcher.

A Study of Tuberculosis in Baltimore, Dr. Buckler.<sup>1</sup>

On the Growth of our Knowledge of Acute Miliary Tuberculosis, Dr. Sowers.

Laennec, Dr. Thayer.

A Review of the Cases of Tuberculosis in the Medical Wards from 1889 to 1899, Dr. McCrae.

The Physical Signs of Pulmonary Tuberculosis, as described by Laennec, Dr. Hamburger.

Villemin and Cohnheim, Prof. Welch.

A Review of the Cases of Tuberculosis in the Surgical Wards from 1889 to 1899, Dr. Bloodgood.

On the Diagnostic Value of Tuberculin, Dr. Tinker.

The History and Work of the Saranac Laboratory for the Study of Tuberculosis, Dr. E. L. Trudeau.<sup>2</sup>

Koch, Prof. Welch.

A Review of the Cases of Tuberculosis in the Gynæcological Wards from 1889 to 1899, Dr. Schenck.

Louis's "Recherches sur la Phthisie," Dr. Florence R. Sabin.

Distinguished American Students of Tuberculosis, Dr. Jacobs.

A Review of Tuberculous Lesions found in the Pathological Department between 1889 and 1899, Dr. H. T. Marshall.

Tuberculosis of the Joints, Dr. J. L. Yates.

At the first meeting of the Society for this year, held November 26, the following programme was presented:

Report on the London Tuberculosis Congress, Dr. Osler.

### ANNUAL REPORT OF INSPECTION WORK IN TUBERCULOSIS CASES—By MISS E. H. BLAUVELT.

The work of visiting the tuberculous patients of the Johns Hopkins Hospital Dispensary came into my hands after the retirement of Miss Dutcher, whose report was read to this Society a year ago. The methods of my work have differed in no important particular from hers, and the conditions found have been the same as those described in her paper.

Every patient of the Dispensary whose disease is diagnosed as tuberculosis is sought for at the address given. A certain proportion have guarded against being found, by giving false addresses. I find thirty-three such on my list. A very few have moved, leaving no trace; but in the majority of cases I have had little trouble in finding either the patient or some member of his family.

These usually receive the visitor in a perfectly friendly manner and are ready to talk freely about the illness and their conditions of life, giving excellent opportunity for instruction as to the communicable nature of the disease and the precautions that should be taken for the benefit of the patient and the safety of others. This advice is almost invariably received in good part by the patients, who profess gratitude for the attention and a purpose to follow the instructions.

The deplorable conditions found in many instances give such sad evidence of the absence of either will or power to improve, that the visitor feels obliged to receive these protestations with a certain amount of reserve. On the other hand, there are a few cases where the eagerness to know and carry out any sanitary measures is most pathetic, and, at the same time, encouraging.

Owing to the early date for the presentation of this report, it is impossible to give a systematic statement of results, and it seems inadvisable to attempt to present to the Society anything but a statistical statement of the visits made and conditions found, following the plan of the report last year.

Miss Dutcher at that time reported her work as carried on till October 1, 1900; so I have included in my report my work to October 1, 1901. At that date I had visited 200 patients. These had occupied during their illness 295 houses.

<sup>1</sup> See JOHNS HOPKINS HOSPITAL BULLETIN for September, 1901, p. 238.

<sup>2</sup> See JOHNS HOPKINS HOSPITAL BULLETIN for September, 1901, p. 271.

Another interesting point is that 104, or 52 per cent, gave an absolutely negative family history as to tuberculosis.

The following summary gives some idea of the conditions found, arranged under the classes of Foreigners, Negroes and American-born whites.

Number of patients visited 300	Foreigners . . . . . 41		
	Negroes . . . . . 57		
	American-born whites. . . 102		
	Foreigners.	Negroes.	American-born whites.
Bad sanitary location. . . . .	39%	39%	7%
Insufficient light and ventilation. . . . .	41%	42%	19%
Overcrowding. . . . .	41%	16%	18%
Personal and household uncleanness. . . . .	34%	33%	17%

The number of foreigners is so small as hardly to warrant a separate rating of different nationalities. The condition of this class as a whole gives decidedly the worst impression, though there are quite as bad individual cases in the other groups.

So long as we continue to import and to allow to grow up

among us so many persons with a marked predilection for dirt, darkness and much-breathed air it is not apparent how this theoretically preventable disease is practically to be prevented. Yet I feel sure that the method followed here has excellent results in some cases, and if the work could be more widespread it is possible that there might gradually be cultivated different tastes, with a consequent improvement in habits and lessening of disease.

The programme of the meeting held December 17 was as follows:

Introductory, Prof. Welch.

The Pathology of Hodgkin's Disease illustrated by the Cases in the Pathological Department, Johns Hopkins Hospital, Dr. Dorothy M. Reed.

Hodgkin's Disease and Tuberculosis, Dr. Joseph Sailer, of Philadelphia.

Some of the Clinical Features of Hodgkin's Disease, Dr. Osler.

## THE JESSE WILLIAM LAZEAR SCHOLARSHIP.

At a meeting of the friends and admirers of the late Jesse William Lazear, M. D., held on the 22d of May, 1901, it was decided to take steps to collect a fund for the establishment of a proper memorial of the man and of his work. As a result of this meeting the following circular was sent to a limited number of physicians:

On the 25th of September, 1900, Jesse William Lazear, at that time Acting-Assistant Surgeon in the United States Army and a member of the Government Commission for the investigation of yellow fever, lost his life from that disease at Quemados, Cuba.

Doctor Lazear was born in Baltimore County, Maryland, in 1866, and graduated from the academic department of the Johns Hopkins University in 1889. In 1892 he received the degree of M. D. from Columbia University. From 1892-95 he spent his time in study and investigation in Europe and as an interne at the Johns Hopkins Hospital in Baltimore. During the following three years and a half, while a member of the staff of the Out-Patient Department of the Johns Hopkins Hospital, he did much valuable work as a teacher and investigator in the laboratory of clinical pathology. In February, 1900, induced by the opportunity for research concerning malarial and yellow fevers, Lazear became an acting assistant surgeon in the United States Army and was assigned special laboratory duties at Columbia Barracks, near Havana. Later, he was appointed member of a special government commission for the investigation of yellow fever. The brilliant discoveries of this commission concerning the etiology and manner of infection of yellow fever have recently been referred to in public by a distinguished pathologist as the most important piece of work by American students since the discovery of anæsthesia. To these results Lazear, as a member of the commission, contributed largely. The final proof of their discovery that the disease is transferred by the bite of a certain mosquito, could only be obtained by direct experiment upon a human being. To this experiment Lazear,

with another of the committee, courageously and heroically subjected himself, and in the performance of this noble duty he lost his life.

The many friends and admirers of the talented and accomplished student, of the brave, true, self-sacrificing man, desire to establish a lasting memorial to him and to his work. To this end a meeting was held on the evening of Wednesday, May 22d, which was presided over by Professor William Osler. At this meeting it was concluded that the nature of the memorial could better be decided upon when some idea could be obtained as to the amount of money available. It was, therefore, decided that a committee consisting of Dr. Stewart Paton and Dr. William S. Thayer be appointed to arrange for the distribution of a circular among the friends and admirers of Lazear, setting forth the object of the meeting. It is earnestly hoped that not only those who have known and admired Lazear and his work, but also others, who appreciate courage and manliness and self-sacrifice, may contribute to the fund for the Jesse William Lazear Memorial.

The plan which recommended itself to the committee was the establishment of a permanent fund to be devoted to the purchase of works relating to the study of tropical diseases, for the Johns Hopkins Hospital library, and also the erection of a tablet at the same hospital in memory of Dr. Lazear.

The response to these circulars was so generous that the committee has been led to hope that if a more general appeal were made a sum might be accumulated sufficient to establish a permanent scholarship for the study of tropical diseases. It has, therefore, been decided to make a fresh appeal to a wider circle.

If it be impossible to obtain a sufficient sum of money to found a scholarship, the committee has decided to establish a library fund and erect a memorial tablet as before proposed.

The committee earnestly hopes that the name of this brave

man who deliberately sacrificed himself for so noble a cause may be perpetuated by a fitting and lasting memorial. And surely no memorial could be more fitting than a scholarship which might enable others to continue the great work to which Lazear gave his life.

Any contributions may be sent to Dr. Stewart Paton, Treasurer, 213 West Monument street, Baltimore, Maryland.

WILLIAM OSLER, *Chairman.*  
STEWART PATON,  
W. S. THAYER,  
*Committee.*

## NOTES AND NEWS.

Dr. A. D. Atkinson, Assistant Resident Physician from 1895 to 1896, is Associate Professor of Clinical Medicine, University of Maryland. Address: 609 Cathedral St., Baltimore, Md.

Dr. Herbert W. Allen, House Medical Officer during 1900 and 1901, is Resident Physician at the Lakeside Hospital, Cleveland, Ohio.

Dr. W. S. Baer, House Medical Officer during 1898 and 1899, and Assistant Resident Surgeon from 1899 to 1900, is Instructor in Orthopedic Surgery, Johns Hopkins University. Address: 21 W. Franklin St., Baltimore, Md.

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## ON A SIMPLE METHOD OF PREPARING EPINEPHRIN AND ITS COMPOUNDS.

BY JOHN J. ABEL, M. D.

(From the Pharmacological Laboratory of The Johns Hopkins University.)

### INTRODUCTORY.

I stated in my last paper<sup>1</sup> that my early empirical formula for epinephrin I had found to be too large by one benzoyl group  $\text{CO}_2\text{C}_6\text{H}_5$ . This was in consequence of the singular tenacity with which this lone radical defied all but apparently destructive methods for its removal from the original benzoyl compound.

Elimination of this retained radical from my former series of compounds and substitution of the displaced hydrogen atom leads to the formula  $\text{C}_{10}\text{H}_{11}\text{NO}_3$  as an adequate empirical expression for epinephrin as prepared by the methods hitherto employed by me.

It has also been shown in my previous papers that the substance which v. Fürth has called suprarenin is in reality nothing else than epinephrin. This suprarenin has thus far been presented only in the form of an impure iron com-

pound for whose composition v. Fürth has not been able to deduce a rational formula.

His analyses show that the iron compound in question as prepared by him is of a variable composition. He, also by comparison with the commercial preparation, adrenalin, assumes that those fractions of his iron compound which show the highest percentage of carbon most nearly represent the true composition of the blood-pressure raising substance. These fractions give an average composition<sup>2</sup> shown by the expression  $\text{C}_{8.5}\text{H}_{12.2}\text{NO}_2$ , an expression that is only a rough approximation to the truth.

By making this iron compound in large amounts I was enabled to prepare from it an acetyl derivative, and, after saponifying it, to obtain enough material to prepare a picrate of epinephrin, from this a bisulphate and to convert

<sup>1</sup> This BULLETIN, vol. xii, p. 337.

<sup>2</sup> Beitrage zur Chemischen Physiologie und Pathologie, Bd. i, S. 243.

this again into an acetyl derivative. This compound gave on analysis data that agreed well with those required for the triacetyl derivative of an oxy-epinephrin,  $C_{16}H_{11}NO_4$ .

The result of this analysis alone suffices to prove that suprenin and epinephrin are one and the same body, except in so far as precipitation with ferric chloride and ammonia, or the conversion of the iron compound of suprenin into its acetyl derivative without first removing its iron, has altered its composition.

In the paper already alluded to I have also maintained that adrenalin is only an impure modification of epinephrin, not fundamentally different. Both Aldrich and Takamine declare adrenalin to be the blood-pressure raising principle in the free state, "the base itself," as Takamine says. Aldrich<sup>2</sup> adopted the empirical formula,  $C_9H_{13}NO_3$ , as representing the elementary composition of his own adrenalin as well as that of the "purified" adrenalin of Takamine. Although this formula is a close approximation to that adopted by me for free epinephrin  $C_{10}H_{11}NO_3$ , it is, as I have shown, no more than an approximation to the truth, since it does not coincide with the analytic data of Aldrich. Furthermore, a study of these data has shown that no rational formula is deducible from them, that adrenalin, in short, as prepared and analyzed by Aldrich, is a mixture and not a chemical individual.

The same remarks will apply to the recent paper<sup>3</sup> by Takamine in which he describes his method of obtaining adrenalin. The average values of his elementary analysis are given in the following table<sup>4</sup> to which is added a calculation of the elementary values of his "probable empirical formula" for adrenalin,  $C_{10}H_{13}NO_3$ .

Found	Required for $C_{10}H_{11}NO_3$
C = 59.39	C = 60.91
H = 7.84	H = 7.61
N = 7.88	N = 7.11
O = 24.89	O = 24.37
100.00	100.00

Comparison of the required values with those actually found shows a deficit of 1.53% in carbon and an excess of 0.77% in nitrogen. No empirical formula can be made to fit these data, a sure proof of the fact that the substance analyzed by Takamine does not consist of a single, pure chemical individual. Crystalline it is, but not pure. Leaving out of consideration the analysis recently published by v. Fürth showing that a commercial specimen of adrenalin contained 57.84% of carbon and 8.11% of nitrogen, the analyses furnished by Aldrich and Takamine give nearly the same values for nitrogen, namely, 7.50% and 7.88%, while the values for carbon are 57.89% and 59.39% in the two cases,

an inexplicable lack of agreement in the analyses of what is evidently one and the same substance.

Takamine, indeed, goes so far as to assert that his formula differs from that of Aldrich by  $CH_2$ .

More than three years ago I showed that the blood-pressure raising principle of the gland could be isolated in the form of active salts and that it was precipitated by ammonia, though in a physiologically inactive modification.

Takamine has precipitated this blood-pressure raising principle also by ammonia directly from a concentrated water and alcohol extract of the gland without previously forming chemical compounds of any sort and has found the resulting product to be crystalline and physiologically active.

Takamine dissolves the brown precipitate produced in the gland extract by ammonia in acidulated alcohol and removes inert substances as far as possible by the addition of ether. He then reprecipitates his substance out of this alcohol ether solution by means of ammonia. This is a method very unlikely to lead to a pure substance, for when a crude precipitate is obtained as above from an animal tissue and thus precipitated, it is highly probable that foreign substances are carried down with the compound which it is designed to throw out, and that in the subsequent washing with non-acidulated alcohol these will not be entirely removed. In support of this statement I need only mention that the commercial specimens of adrenalin that I have examined retain a sufficiently large amount of a phosphorus-containing substance to make their analysis impossible. One has only to fuse three or four grains of it with pure caustic potash and potassium nitrate in order to obtain with molybdic solution a very considerable precipitate of ammonium phosphomolybdate. In order to leave no doubt that we are here dealing with phosphorus I made control tests to prove the purity of my reagents and also transformed the phosphomolybdate referred to into the characteristic ammonia magnesium phosphate. I judge from the bulkiness of the phosphomolybdate precipitate that a quantitative experiment would result in a high percentage of an impurity.

#### ON A METHOD OF OBTAINING COMPOUNDS OF EPINEPHRIN.

Convinced that the properties of epinephrin, as described by me, are inherent characteristics of the substance and that when they are not immediately apparent it is because some chemical modification has taken place, I sought new methods for the preparation of epinephrin in which the use of benzoyl chloride and the employment of the autoclave should be avoided.

Epinephrin as well as the modifications of it called adrenalin and suprenin are all precipitated out of solution in acid alcohol with ammoniacal zinc chloride in the form of a flocculent white compound. v. Fürth was the first to make use of this salt as a precipitant of the substance that he obtained by decomposing a basic lead acetate precipitate from gland extracts with concentrated sulphuric acid, the precipitate being suspended in methyl alcohol.

<sup>1</sup> Amer. Journ. of Physiol., vol. v, p. 457.

<sup>2</sup> Amer. Journ. of Pharmacy, vol. 73, p. 523.

<sup>3</sup> I have corrected the arithmetical errors made by Takamine in calculating his averages.

In making an ammoniacal zinc chloride solution the basis of a method of isolation I determined to avoid the use of strong mineral acids and to employ hydrogen sulphide, both for the removal of zinc and for its reducing action and to end with ammonia as a precipitant exactly as in my first work.

The material that I started with consisted of the concentrated aqueous extract of 46 pounds of beeves' glands, or 3 gallons of a thick, turbid fluid, of grayish-white appearance. The filtrate is at first straw-colored but soon changes to a darker tinge on exposure to the air. This extract was prepared for me by Armour and Company of Chicago, and I take pleasure in again thanking this firm for their continued liberality in supplying my laboratory with expensive products of this kind.

This extract was prepared for me, like those formerly used, by repeatedly extracting the finely-divided glands at a moderate temperature with barely acidulated water, acetic acid being used in this instance. The extracts thus obtained were now brought to the boiling point for a moment to coagulate proteids as far as possible, then filtered and immediately concentrated under diminished pressure to the volume of 3 gallons. In extracting the gland I have made use of various acids, organic and inorganic, and have come to the conclusion that it makes no difference what acid is employed provided only that it is not an oxidizing acid and that it is used in *very great dilution*, as otherwise a peculiar converting action will be exerted by the mineral acids at least in the subsequent concentration. The change produced by strong mineral acids will be described at length in a later section of this paper.

In the original extraction it might also be well to steep the finely divided glands for a period of some hours in a vacuum apparatus at a temperature of 45° C., supplying water as fast as it distills off and keeping the whole mass in agitation the while, then filtering with a pressure apparatus until only a dry pulp remains.

The thick grayish fluid, above described, is filtered under pressure and thus a second time freed from a large amount of inert material. Three liters, for example, of this fluid were concentrated at a temperature of about 45° C. to a volume of 200 cc. This solution is poured into a tall cylinder, absolute ethyl alcohol<sup>6</sup> is added in small quantities at a time with constant and vigorous shaking until 1800 cc. of the absolute alcohol<sup>7</sup> have been added. At the conclusion of the operation the cylinder contains a large amount of a sticky precipitate which becomes granular in the course of time while the alcoholic solution has a light straw-colored tinge. After standing a few hours the alcohol is separated from the precipitate and distilled off under diminished pressure. A

straw-colored syrup, which, on cooling, congeals to a clear golden-colored pitch, remains. This dissolves almost completely in an ammoniacal zinc solution. In repeating the experiment with the quantities described I have stopped the distillation when the volume of syrup reached about 60 cc. and while it would still flow freely. The solution in the zinc mixture is so complete that filtration is not necessary.

The ammoniacal zinc solution is now precipitated by the gradual addition, while stirring, of eleven volumes of absolute alcohol and set aside for some hours. During this period only a very slight increase in precipitation occurs. The precipitate, which for convenience may be labeled Zn I and which consists of a heavy, slightly reddish-yellow mass is removed, dried at 50° C. and powdered. It contains much epinephrin but a considerable amount remains also in the alcoholic filtrate, since the solubility of its zinc compound in strong alcohol is evidently increased by the presence of jecorin and other substances soluble in alcohol. This filtrate is now concentrated under reduced pressure, a little only of the fluid being poured into the flask to start with and the rest supplied continuously as the distillation proceeds, the object of this being to carry off water as far as possible in company with the alcohol. When this alcoholic solution has been reduced to a volume of 50 or 60 cc. absolute alcohol is added until its volume reaches 100 cc.; three volumes of ether are now added in small portions at a time, with vigorous agitation, and immediately a sticky, ropy precipitate is found adhering to the bottom and sides of the vessel. This precipitate we will designate as Zn II. The very little epinephrin remaining in the alcohol-ether mixture is deposited in the course of time.

#### PROPERTIES AND FURTHER TREATMENT OF THE ZINC PRECIPITATES.

We now have the epinephrin of the gland in the form of a zinc compound in two precipitates, Zn I and Zn II. The former, when dried and powdered, has the appearance of slightly discolored flour; the latter might perhaps also be dried and powdered, but no attempt was made to alter its appearance. Zn II is small in bulk as compared with Zn I and dissolves with the greatest ease in very dilute acetic acid while Zn I requires repeated treatment with the same for its solution. It of course contains much besides the zinc compound of epinephrin, as is probably also the case with Zn II, but nevertheless it can be almost completely dissolved by the above method.

The combined fluids required to dissolve Zn I and Zn II amounted to 250 cc. and contained only enough acetic acid to effect the solution.

The zinc was now removed with sulphuretted hydrogen, and the resulting zinc sulphide washed until the filtrates gave only a slight reaction for epinephrin with ferric chloride. The original filtrate and the washings were reduced under diminished pressure to about 30 cc. when a fluid of a somewhat reddish color, but entirely transparent, was obtained.

<sup>6</sup> In some of my earlier work, I made frequent use of methyl alcohol as a precipitant and found that it answered the purpose equally well.

<sup>7</sup> I have also used zinc chloride in alcohol at this stage to precipitate foreign substances, but have not yet carried this solution through to the end.

## BEHAVIOR TOWARD EXCESS OF AMMONIA.

When to a beaker containing the above fluid ammonia of specific gravity 0.944 is added until the reaction is plainly alkaline, no change is produced, except that the clear solution becomes slightly redder. If now this strong ammonia is added boldly in such a manner that it flows down the sides of the beaker, a striking change soon takes place.

At the line of demarkation between the two liquids a white turbid zone appears which soon resolves itself into a mass of crystals which fairly rain to the bottom of the beaker. On being stirred with a glass rod, the fluid becomes a mass of crystals and the odor of ammonia which before was intolerably strong, entirely disappears. The solution is still strongly alkaline, but the reaction has only begun; fresh portions of ammonia are added only to be absorbed in turn as each new crop of crystals falls to the bottom or adheres to the sides of the flask. The reaction is not complete until the striking avidity of the solution for ammonia is entirely satisfied, in short until the solution smells strongly and permanently of ammonia. At this time the fluid above the crystals is of a light straw color, but in a short time it takes on a pink tinge due to the oxidation of the epinephrin that still remains in solution, and this color deepens during filtration, which should immediately follow the operation just described. If filtration be delayed for a day, the supernatant fluid becomes black and a not inconsiderable loss occurs from resolution and oxidation of the precipitate. Once prepared the compound may be repeatedly crystallized out of its solution in hydrochloric acid by the free addition of ammonia with slow stirring.

## ON THE EFFECT OF GRADUAL ADDITIONS OF AMMONIA AT INTERVALS OF TIME.

In my first trial I made the solution plainly alkaline with ammonium carbonate, added what I feared was an excess of ammonia and set aside overnight. The next morning only a thin layer of crystalline nodules was found at the bottom of the beaker with a very dark-colored fluid above. These crystals were removed and washed with water and more ammonia was added to the now somewhat diluted filtrate. On stirring with a rod and again setting aside, an abundant crystalline precipitate fell out of the dark fluid. On repeating the filtration and again adding ammonia, the same result followed. This avidity for ammonia observed in solutions prepared as above, although they were all the while strongly alkaline, led me to the bolder use of ammonia.

In a later paper I shall discuss at more length the chemical reactions that are involved in this liberal use of ammonia and shall attempt to show why epinephrin is here precipitated in the form of a crystalline substance. v. Fürth has maintained that the substance with which I have been so long working cannot be the blood-pressure raising prin-

ciple of the gland for the reason, among others that have also been refuted, that in its native state as found in an aqueous extract of the gland, it is not precipitable by ammonia. I was able to show in reply to this criticism that every compound of epinephrin is precipitated in its flocculent, inactive state by ammonia if it has first been subjected to hydrolytic treatment, while at the same time I admitted the truth of his statement that the native product is not precipitated by ammonia and this, it is now seen is true only for the dilutions with which he and I were then working.

A year ago I subjected the suprarenal glands to the action of the papoid ferment, made extracts of the digested mass by the use of water and a series of organic fluids and treated the resulting products with ammonia and ammonium carbonate, always making plainly alkaline and setting aside. The result was always unsatisfactory, only a very minute amount of substance mixed with oxidized epinephrin and foreign material being obtained. My later experiments showed me that an abundance of ammonia is required and that the active principle must be present in the solution in large amounts.

The substance as thrown out by ammonia is strongly basic, it also reduces Fehling's solution with precipitation of cuprous oxide. The cause of this changed behavior toward Fehling's solution after exposure to the action of ammonia will also be discussed in a subsequent paper.

In its behavior toward Fehling's solution, ferric chloride silver nitrate and a few other reagents, it agrees with my former preparations, but unlike these it fails entirely to give the alkaloidal reactions that characterize epinephrin. I shall soon publish analyses that will show to what extent this crystalline substance agrees in composition with the similar and probably identical compound contained in the material analyzed by Aldrich and Takamine.

## CONVERSION OF THE SUBSTANCE ISOLATED BY THE ZINC PROCESS INTO EPINEPHRIN.

Whatever differences in elementary composition may be found to exist between this substance and epinephrin,  $C_{10}H_{11}NO_3$ , it is certain that the former may easily be converted into a physiologically active substance that gives all the characteristic reactions of epinephrin. The following experiment will illustrate this conversion:

*Epinephrin Hydrochloride.*—One gram of the crystalline compound, after being twice recrystallized and freed as far as possible of the alkaline gas which is constantly being evolved from it, was dissolved in 1 cc. of hydrochloric acid of specific gravity 1.19 and absolute alcohol was added to the volume of perhaps 20 cc., the solution continuing to be perfectly clear, though of a slightly reddish tinge. 80 cc. of ether was now added in small portions at a time until no further precipitation of epinephrin hydrochloride occurred. The precipitate was now dissolved in a small volume of absolute alcohol and again precipitated by ether. As thus prepared, this salt falls out in the form of white masses and separate particles which

\* I employed ammonia free of pyridine which, however, is not at all necessary for the success of the experiment.

cling to the bottom and sides of the vessel. It is transferred rapidly to a filter, washed with a mixture of alcohol and ether in which it will not dissolve and then immediately transferred to a desiccator and dried in vacuo.

*Epinephrin Sulphate or Bisulphate.*—This salt is made in the same way, being first dissolved in as little strong sulphuric acid as possible of about 90%.

It is likely that much weaker sulphuric acid than the above will effect the transformation into epinephrin, my object in using acid of this strength was to avoid an excess of water in order that the epinephrin sulphate might not be precipitated in a gummy state.

Both salts are extremely hygroscopic, so long as traces of ether still cling to them. When precipitated in alcohol by ether with the greatest possible exclusion of water, their appearance, when examined with a pocket lens through the flask is suggestive of the micro-crystalline state. Whether these salts are really crystalline can only be determined by precipitating in the field of the microscope. Once exposed to the air, while still moist with alcohol or ether, they lose their crystalline character, if indeed they ever possessed it.

After being thoroughly dried, both salts may be reduced to a white powder. Both salts have now lost their hygroscopic quality, both are very soluble in water and behave like acids toward litmus, a behavior which cannot be due to adherent acid used in their preparation. Experiments in the way of crystallizing these salts are now being made.

From the concentrated aqueous solution of these salts a picrate may easily be formed, and from this I expect to derive salts of other organic acids.

As tested in dilute solution these salts are found to have a powerful constricting action on the blood-vessels of the conjunctival sac. As one affinity is not neutralized by a retained benzoyl group, I entertain the hope that they will surpass the members of my former series in physiological activity and even that of the sulphate of doubtful purity derived from a basic lead acetate which was tested by Professor Reid Hunt.\* The therapeutic importance of such very soluble and stable salts of epinephrin is apparent.

#### BEHAVIOR OF THESE SALTS OF EPINEPHRIN TOWARD ALKALOIDAL REAGENTS.

Mandelin's reagent applied to the dry substance gives the characteristic and delicate play of colors from a yellowish-red to an olive-green formerly described in the case of the mono-benzoyl series.

Stirring a crystal of potassium permanganate into a solution of the dry substance in concentrated sulphuric acid gives rise to a rich plum color. Adrenalin also gives this reaction.

Picric and tannic acids, solution of iodine in potassium iodide, iodine trichloride, phosphotungstic acid (one part to 20 of water with a little hydrochloric acid), and phosphomolybdic acid, all give precipitates, some of them in solutions

of the greatest dilution. Stronger solutions are also precipitated by gold chloride, platinum chloride and by zinc chloride in 50% solution.

This list can no doubt be greatly extended, but for the present it will suffice to illustrate the remarkable action of strong acids in thus altering the character of the original substance.

These salts of epinephrin also differ in another noticeable way from the substance made by the zinc process. On the addition of lime water to equal quantities of each, the odor of the conine-piperidine-like base, to which I have so often referred rises very quickly from the latter, but only after a considerable time, from the former.

*Action of Ammonia on the Salts of Epinephrin.*—Equally striking is the changed behavior of this epinephrin toward ammonia. The addition of this reagent to an aqueous solution of these salts results not in a crystalline precipitate of strongly basic character but in the immediate production of a yellowish-white flocculent precipitate which easily re-dissolves on the addition of strong ammonia. This solution rapidly darkens and if it is sufficiently concentrated in the first place, a reprecipitation in the form of nodules or granules occurs. I take it that this reprecipitate is an oxidation product of the original flocculent precipitate.

If the flocculent precipitate is rapidly transferred to a filter and washed with cold water, alcohol and ether it may be obtained in the form of a gray powder. This has not yet been tested as to physiological activity, but it agrees in all its other characteristics with the corresponding mono-benzoyl epinephrin of my former papers. It still retains its power to reduce copper sulphate and shows all the other reactions of epinephrin.

We are ignorant of the state in which the blood-pressure raising principle exists in the gland. We have seen that under the influence of strong ammonia it falls out of an extract of the gland as a crystalline compound of markedly basic properties and that exposed to the action of acids it is changed to an apparently very different substance of feebly basic or acid properties.

We have also seen that the former variety may easily be changed to the latter by exposure to the action of acids. The reconversion has not yet been effected, but I hope to accomplish this also, or at least to throw light on the chemical process involved in the first conversion.

*Note on the Character of the "Autoclave Effect."*—The described action of sulphuric and hydrochloric acids on the modification of epinephrin isolated by me by the zinc process throws light on what I have hitherto called the autoclave effect. In my early work on this subject I made use of this apparatus in the saponification of my benzoyl derivative with dilute acid and I did so to avoid oxidation as far as possible. In consequence of the temperature used, the dilute acid that was used as a hydrolyzing agent acted as do strong acids at room temperature in the experiments above described.

\* Am. Journ. of Physiol., March, 1901.

ON THE DECOMPOSABILITY OF THE CRYSTALLINE DERIVATIVE OF EPINEPHRIN AS PREPARED BY THE ZINC PROCESS AND BY OTHER STILL SIMPLER METHODS.

An alkaline gas is continually being evolved from the crystalline derivative at room temperature, as the following experiments will prove:

*Exp. I.* A small portion of the compound as made by the zinc process was twice crystallized out of its solution in dilute hydrochloric acid by the free addition of ammonia, a small amount being taken to insure perfect washing. After the last crystallization, the material weighed about one gram.

It was washed with water until no trace of chlorine could be detected by silver nitrate and nitric acid, either in the filtrate or in the substance itself. The products of the energetic oxidation that results on boiling with these two reagents will be the subject of a later paper. The substance was next washed with absolute alcohol, then with ether and exposed at room temperature until dry. It was now spread out on a watch glass and a second watch glass placed over it, to whose inner surface a strip of moist red litmus paper was attached. In the course of two hours the free edges of the strip had turned blue.

*Exp. II.* A larger portion of the substance, about 6 grams of finely crystallized material was recrystallized and washed in the manner just described until the absence of chlorides was assured, the washing being continued for some time even after it might safely have been assumed that no free ammonia was present.

As fresh amounts of water were added, the material was frequently stirred with a glass rod, and the freely-dripping filtrate was each time drawn off by gentle suction. A brief washing with absolute alcohol then followed and the substance was spread out on the bottom of a crystallizing dish which was placed under a similar vessel containing 10 cc. of sulphuric acid of such strength that 50 cc. contained three drops of 25% sulphuric acid and gave a bright red color to a litmus solution. Over this a bell jar was placed. In a short time a change in the tint of the litmus solution was observed and twenty-four hours later it had assumed a distinctly blue color. When this dilute sulphuric acid was replaced by a fresh portion, it also was made alkaline in the course of twenty-four hours. After standing a week it seemed to yield about as much of the alkaline vapor as at first. On boiling with water a portion of the substance that had been thus exposed over dilute sulphuric acid I observed a further liberation of ammonia.

*Exp. III.* The adrenalin of commerce gives off even more of this alkaline gas than does the preparation above described. One has only to make the watch-glass test with 60 mg. of this substance in the dry state to find the strip of moistened red litmus paper used turn entirely blue in a short time.

It is evident that we are here dealing with a very decomposable substance, not a stable one as Aldrich and Takamine

have stated it to be. Add to this fact that commercial adrenalin is rich in phosphorus and that the published methods of preparing it do not guarantee the absence of phosphorus-containing compounds and we have a full explanation of the illy concordant analytical results which these observers have obtained.

I assumed in my last paper that the so-called adrenalin is in reality impure epinephrin,  $C_{16}H_{11}NO_3$ , in the free reduced state, and I offered several suggestions to explain why Aldrich's analyses did not square with the above formula, calling especial attention to the high nitrogen content of his substance. It now appears that both Aldrich and Takamine have tried to analyze a substance which is constantly giving off nitrogen in the form of an alkaline gas. Aldrich, indeed, dried his substance over sulphuric acid in vacuo.

ON THE NATURE OF THE ALKALINE GAS EMITTED BY THE COMPOUND.

In the absence of analyses it is not as simple a matter as might be supposed to identify the alkaline gas referred to, or, what is more important, to state in what form it leaves the gland. I placed a filter containing about 10 grams of freshly-prepared but moist material made by the zinc process and thoroughly washed into a desiccator charged only with calcium hydrate, and 12 hours after, it was found to be filled with an alkaline gas which had an odor like that of ammonia. But if to the dilute sulphuric acid used in Experiment II sodium hydroxide be added, an odor is obtained like that of methyl amine, that is, both ammoniacal and fishy. And yet if, to even large amounts of the substance which has been long exposed to air, sufficient sodium hydrate be added to dissolve it, neither the ammoniacal nor the fishy odor arises. At room temperature no odor whatever is given off by this alkaline solution for the first few moments, but if it is gently warmed, the characteristic and offensive odor of the substance that I have called the coniine-piperidine-like base becomes evident. This simple experiment suffices to prove that we are not dealing here with a simple but easily dissociable ammonium salt of epinephrin, not at least after the substance has been exposed to moist air for a long time.

Later I observed that if the dilute sulphuric acid be removed entirely from the bell jar in Experiment II, the substance itself will give off this same coniine-piperidine odor. It is impossible to dry our substance in a drying chamber even at a low temperature, at least in the presence of air without losing much of this odoriferous constituent, as the drying oven soon becomes filled with its fumes. It has also been shown in this paper that this crystalline derivative of epinephrin emits this volatile gas much more easily on the addition of lime water than does the epinephrin into which it is converted by mineral acids when treated in the same way.

I have shown in an earlier paper<sup>10</sup> that this volatile base

<sup>10</sup> Zeitschr. f. physiol. chem., Bd. xxviii, S. 344.

undergoes decomposition when we attempt to distil it from an alkaline aqueous solution. From all that has been said above it would appear probable that the alkaline gas which is spontaneously liberated from the crystalline base owes its origin to that part of the molecule which I have called the coniine-piperidine-like substance and that this substance undergoes further decomposition into a primary amine or some other ammonia base, according to the circumstances of the case. This is not meant, however, to exclude the possibility of the formation of a dissociable ammonium salt in the first instance.

#### ON SIMPLER METHODS OF PREPARING THE COMPOUND UNDER CONSIDERATION.

Both Aldrich and Takamine state that other alkalis may be used in place of ammonia in precipitating their adrenalin, but that ammonia is to be preferred because of the solubility of adrenalin in fixed alkalis. On making free use of ammonia, I found that a very fair yield of the substance could indeed be obtained from a concentrated aqueous extract of the gland without the use of zinc hydrate, ferric chloride, lead acetate, precipitation with ether or other methods of purification. These measures are entirely unnecessary as far as the mere precipitation of the substance is concerned, although, of course, so pure a substance is not obtained as when the zinc process is used.

Only two operations need precede the use of ammonia or other alkali: evaporation of an aqueous extract of the gland, the preparation from this of an alcoholic extract and the removal of its alcohol. After this last step the free use of ammonia results in the formation of the same crystalline compound described above with the same accompaniment of ammonia absorption by the alkaline solution. Experiments made more than a year ago lead me to suspect that absolute alcohol saturated with ammonia or containing the fixed alkalis will not precipitate our substance out of its solution in strong alcohol, or at least only imperfectly; in other words, that the presence of water is necessary to the success of the reaction.

#### ON THE SUBSTITUTION OF OTHER ALKALIES FOR AMMONIA AS A PRECIPITATE.

*Exp. I.* On adding to the water-alcohol extract just described a 25% solution of potassium hydrate, no change was at first produced, the solution did not change color nor did it give off the odor of ammonia nor of a primary amine. In a few moments, however, a precipitate began to fall out. After prolonged washing with water and alcohol it was obtained as a snow-white powder, which, when examined under the microscope with a low power, appeared to be amorphous. In its chemical behavior it seemed to be identical with the substance obtained by the zinc process. Like that it also evolved an alkaline gas.

*Exp. II.* Thinking that it might possibly be contaminated with some other constituent of the gland which had

united with the alkali and formed an insoluble compound with it, I made the following experiment:

Two grams of the twice crystallized compound made by the zinc process, a compound which certainly appears to be a definite, although highly unstable chemical individual, was dissolved in a requisite and known amount of dilute sulphuric acid. This was at first neutralized by the addition of 1/10 N potassium hydrate, but seeing that the solution would become too dilute for the purposes I had in view, I added a 25% solution of the hydrate, drop by drop, until the precipitate that had fallen out in consequence of the neutralization of the sulphuric acid employed, had entirely redissolved.

Of course a considerable excess of potassium hydrate was now present in the solution and this had assumed a dark brown color. Ammonia in excess was now added, and in the course of an hour or two about half of the original material had crystallized out in the form of small prisms clearly visible with a pocket lens.

*Exp. III.* Calcium oxide was added in small quantities to some of the material used in Exp. I. As soon as the fluid was saturated with this alkali, it became turbid and a little of the compound under discussion fell out. Further experiments showed that the crystalline base made by the zinc process is to a very large extent soluble in lime water at room temperature. Only material that had long been exposed to air was used, and such material always leaves a residue which does not dissolve in further amounts of lime water. On the addition of ammonia to such a solution in lime water no precipitate is produced, but if much alcohol and then ether is now added, a dark flocculent precipitate of amorphous epinephrin soon falls out. Further experiments will throw light on this peculiar action of ammonia in the presence of calcium hydrate and will show the relation that exists between this experiment and those described in connection with the action of mineral acids.

I will add that in Experiment I, ammonia was added to the filtrate after the removal of the potassium-containing precipitate and a further amount of the substance equal in bulk to that previously thrown out by the fixed alkali was obtained. The above experiments suggest the possibility of forming a series of alkali derivatives.

I have described a sufficient number of experiments in proof of the fact that the crystalline derivative of epinephrin prepared by the zinc process and by other still simpler methods is a highly unstable substance, that it evolves an alkaline gas at room temperature, that it can be converted by the help of mineral acids into epinephrin itself, although possibly into a form richer in nitrogen than that of my former series. It might seem to be in order to give a more definite expression of opinion as to the true rôle played by ammonia and other alkalis in the experiments described and also as to the relationship that exists between epinephrin and the crystalline compound from which it is derived. Similar relationships are well known to chemistry and a number of possibilities present themselves by way of explanation. I

prefer, however, to await the outcome of my analytical work before committing myself to anything further than a statement of facts.

#### SUMMARY.

1st. The blood-pressure raising constituent of the suprarenal gland may be isolated by the method described in this paper in the form of a basic, minutely crystalline though unstable compound which agrees in some of its properties with the substance that I have called epinephrin, while it fails to exhibit certain other equally fundamental and characteristic properties of this substance.

2d. Mineral acids, however, easily convert this substance into one which is physiologically active and which also gives

all the characteristic reactions of the epinephrin,  $C_{10}H_{11}NO_3$ , contained in my former series of compounds. Highly soluble and apparently stable salts of therapeutic and chemical importance are therefore easily made.

3d. Analyses of the substances described will soon be given to show what changes, if any, in elementary composition take place under the influence of the acids used in the conversion; also how these new compounds of epinephrin will agree in composition with those of my former series; also, how far the substance isolated by the zinc process agrees in composition with the similar and probably identical compound contained in the material analyzed by Aldrich and Takamine.

## A NEW COMBINED ELECTRO-CAUTERY INCISOR FOR THE BOTTINI OPERATION FOR PROSTATIC OBSTRUCTION.

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Although the electro-cautery operation was brought out by Bottini as far back as 1876, it was not generally adopted until 1897, when Freudenberg presented to the profession a greatly improved instrument, and followed it up by numerous convincing articles. During the past four years this operation has been performed very extensively, and we are now in a position to stop a moment, look over our results, and discuss the shortcomings of the operation, as well as its merits.

Freudenberg's large collection of operated cases probably shows very accurately the value of the procedure. The statistics are as follows: 752 cases, in which the result was good in 86½%, a failure in 7½%, and the mortality between 1 and 6%.

These figures, if correct, undoubtedly show much better results than can be claimed for any other operative procedure. Castration, while peculiarly effective in a certain class of cases, has been woefully unsatisfactory as a routine procedure, and has justly been relegated to the list of operations historically interesting, but practically valueless.

Prostatectomy thoroughly performed is undoubtedly an operation of great value. There is no question that the statistics as to the value of this operation are entirely misleading, for many reasons; principally because in most of the recorded cases (and in all until recently) the operation was entirely inadequate—merely a nipping off of the most evident intravesical projections, leaving the equally important parts of compression in the deep urethra untouched. There is no question, however, that a thorough removal of the entire gland, which can generally be easily accomplished by enucleation with the finger, is a very successful operation, and entirely satisfactory when perfectly accomplished.

There are, however, several varieties of prostate which are unsuitable for this operation, principally the small and the sclerotic varieties. This, however, is not the principal objection, but the fact that in the majority of instances we are confronted with patients too old and too feeble to safely undergo the shock of a satisfactory prostatectomy. It is for just this class of cases that the Bottini operation has proved such a blessing, and has achieved really wonderful results. On account of the success of the cautery operations in the otherwise hopeless cases, it has become more and more the question whether it should not become the method of choice in all manner of cases. Since there are, however, a certain number of failures (10% or more) and a certain mortality (between 5 and 8%) shown by the Bottini operation, it still remains questionable whether it should replace prostatectomy, especially in younger patients. To settle this point more extended investigation is necessary. It also behooves us to study the causes of failure and fatality in the Bottini operation, with a view of finding means of obviating both as far as possible.

Among the causes of death besides uremia, shock, sepsis, etc. (presumably unavoidable), we find recorded several not unavoidable reasons, principally from improperly placed or too lengthy incisions. In the first category are deaths from the cautery blade burning its way into the rectum, due, as has been shown by Freudenberg, to the fact that the beak of the instrument became caught in a post-ureteral pouch, which is separated by only a short space from the rectum. In the same class are those fatal cases in which the entirely useless anterior cut was made and penetrated (as might have been expected) into the space of Retzius. In the second category are a number of cases in which the operator has

rashly made his incisions too long, resulting in the rupture of the urethra in front of the prostate, and sometimes fatal hemorrhage from division of perineal vessels.

The statement of certain writers that incisions of  $4\frac{1}{2}$ , 5 or 6 cm. in length were often necessary to remove the obstruction is absolutely without pathological substantiation, and undoubtedly liable to lead to a great many serious blunders in the profession. Very rarely, even in the very largest hypertrophies, should an incision over  $3\frac{1}{2}$  or 4 cm. be made, first because it is unnecessary, and secondly because it is dangerous. Deaths from any of the causes outlined above are preventable, and should in the future be eliminated from the statistics.

In Freudenberg's statistics, after excluding the fatal cases (4.2%), we find 92% improved, 55% cured, 37% definitely improved, and 8% failures. Why should there not be a greater uniformity of results? Is the operative technique, or the instrument at fault? Turning to the instrument, we find the one of Freudenberg much preferable to that of Bottini, as has been very frequently pointed out. But there are several very evident weaknesses in even the former instrument. In the first place, since there is the greatest difference as to size, shape and condition among hypertrophied prostates, it is unreasonable to expect one single cautery blade to be suitable for all. An incision which is plenty deep for a medium-sized hypertrophy may be wholly inadequate for a very large one, and positively dangerous for the small fibroid forms. Then, again, one lobe is often very greatly enlarged while another is only slightly so. Are we, then, to give each the same depth of cautery incision? I have in my collection of autopsy specimens several prostates with small but very obstructive middle lobe enlargements, where the ordinary Freudenberg and Bottini instruments would have penetrated beyond the capsule and perhaps into the rectum.

It is very evident, then, that an instrument with several easily interchangeable blades of graded sizes would be a decided improvement.

There are two other defects in Freudenberg's apparatus which, while apparently trivial, are of considerable importance. The first is in the shape of the beak of the instrument as now constructed. The traction necessary to hold the beak up against the prostate during an operation will often pull it into the urethra. This is due to the fact that the beak meets the shaft at such a wide angle (or at such a slope) [see Fig. 7] that even moderate traction causes it to ride over a median bar (for example) and slip into the prostatic urethra. The dangers of this accident are not small. Indeed it has occurred several times, and has been responsible for several deaths, the cause being division of the membranous urethra, extravasation, hemorrhage, etc. In order to be certain that the beak of the instrument is against the prostate, and has not slipped into the urethra, Freudenberg has wisely advised that a finger be inserted into the rectum to determine its location before an incision is begun.

I have carefully followed this practice for the past two years, and have thus prevented several accidents, for in numerous instances have I found that a little steady traction (as in an operation) would draw the beak into the urethra. But this safeguard is not always sufficiently accurate, for while it is comparatively easy to feel the tip of the instrument turned downward toward the trigone, one cannot often feel the beak with sufficient certainty when the instrument is turned to make a lateral cut, as one of my own cases demonstrated to my sorrow (Freudenberg's instrument was being used). The forefinger of the right hand was inserted into the rectum, and the tip of the beak definitely located to be in the bladder. The rotation was made for a lateral cut, and with the finger still in the rectum traction put upon the instrument to draw the beak up snugly against the prostate. The beak was not felt to slip into the urethra, but before beginning the cautery incision another careful examination with the finger (which was kept in the rectum during the entire operation) was made and did not reveal any slipping of the beak. Despite all these precautions (which happened to be unusually carefully taken in this case) an incision of  $3\frac{1}{2}$  cm. was followed by a gush of blood from the meatus, and a perineal section done under cocaine revealed a ruptured membranous urethra, and extravasated blood behind the triangular ligament. A timely operation saved his life, but it brought very forcibly to my mind the need of a beak which would not slip into the urethra, one more nearly at right angles to the shaft.

The other defect, at times quite disagreeable, was that the handle of the instrument would often become so greatly heated as to burn the hand of the operator, and sometimes to prevent his turning the contact screw to break the electrical current. Examination soon showed that this was due to bad contact. This connection was made by a flat surface coming against a cylinder, resulting in a linear contact, insufficient to conduct the high current necessary to heat the instrument without itself getting hot. This defect, while merely one of mechanical construction and easily remediable by bringing broader areas into contact, was one which frequently led to great trouble both on account of the heating of the handle and the insufficiency of the electrical current which reached the cautery knife.

Recognizing more and more during two years' work with Freudenberg's instrument the drawbacks referred to, and especially, feeling the need of blades of different size, the writer finally consulted the Kny-Scheerer Co. of New York,<sup>1</sup> during April, 1901, with reference to the construction of an instrument which would, if possible, fill all the requirements. After considerable experimentation we have produced, we believe, a satisfactory instrument, the construction of which is thoroughly explained by the accompanying cuts.

As seen in the illustrations, the form of Freudenberg's

<sup>1</sup> My thanks are due to Mr. Charles Farnar, mechanic, for valuable help.

instrument is adhered to (Fig. 1), the only changes being in its having four interchangeable blades, a beak of different angle, a connecting handle with more extensive contact surfaces, and a few minor changes in construction. By a very simple device, the simple elevation of a sliding bar on the rotary wheel, one blade may be removed and another inserted

Blade No. 3 corresponds to the one usually found in Freudenberg's instrument, and is the one most generally used, while No. 2 is useful in small hypertrophies, and No. 4 for the very large. Blade No. 1 (the smallest) was constructed mainly to complete the set, and without any idea of much practical value. I have been surprised, however, to

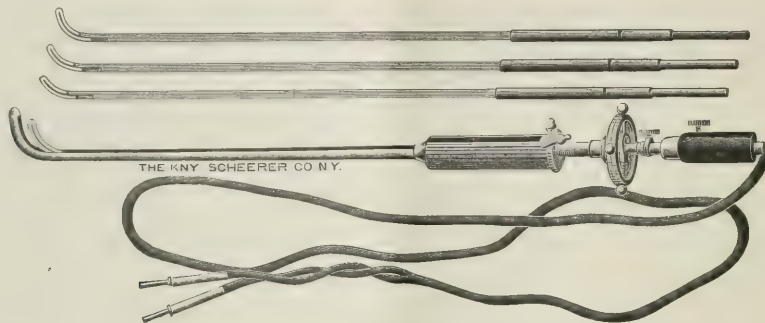


FIG. 1.

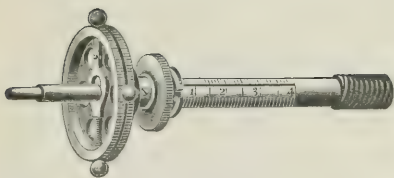


FIG. 2.

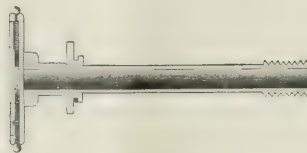


FIG. 3.



FIG. 4.



FIG. 7a.



FIG. 6.



FIG. 7.

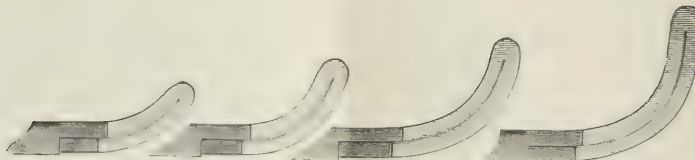


FIG. 5.

(Figs. 2 and 3). The sliding bar working on a spring holds the rod containing a blade firmly attached to the screw mechanism by engaging the circular groove near its outer end (Fig. 4). We have had four blades constructed as shown in Fig. 5. The smallest having an elevation of .8 cm., the second 1.2 cm., the third 1.7 cm., and the fourth 2.1 cm.

find it very useful in several cases, which will be given in detail further on.

The change in the shape of the beak has been of very great comfort. The new beak (Fig. 6) cannot possibly slip by the prostatic orifice into the urethra with all the outward traction which may be put upon the instrument during

the operation, whereas with the Freudenberg instrument (Fig. 7) one must be constantly on his guard lest this occur. The right-angled character of the beak does not make it any harder to introduce, in fact it seems to ride over a high median bar with greater ease, having more the shape of a prostatic catheter.

The changes made in the instrument handle of the conducting cable, as shown in the diagrams, consist merely in bringing larger surfaces into closer and firmer contact. To accomplish this we have placed beneath the end of the contact-making thumb screw a metal spring, having on its end a concave contact block (see Fig. 7a) made to fit the circumference of the end of the male blade. Another thumb screw has been placed at the end of the handle to insure tighter contact at the other connection. These changes have completely done away with the disagreeable over-heating of the contact screw, which constantly occurred before, and which was undoubtedly due to insufficient contact, as described above.

During the past five months I have used this instrument on sixteen cases, and have amply proved it to be practical, and one, I think, that has overcome many of the defects to be found in Freudenberg's instrument.

We will give in abstract a few illustrative cases, but before doing so it may be well to state the measures we take to determine before operation the size, shape and character of the prostatic enlargement, and consequent selection of the blade to be used, and the length of the cuts.

Besides a systematic general physical examination, noting particularly the condition of the arteries, a very careful local examination is made as follows: *Rectal examination*, noting: the size, shape and consistence of the prostate; the relative enlargement of the two lobes, the thickness of the prostate as revealed by the finger in the rectum, and a sound in the urethra (determining in this way the thickness of the hypertrophy in the median portion); the adnexa of the prostate, vesicles, glands, rectal mucosa, etc. *Bladder examination*: 1. with catheter, noting the location, depth and character of prostatic obstruction, with residual urine, the capacity of the bladder and its tonicity. 2. With the cystoscope, noting: (a) the size, shape, location and character of intravesical prostatic hypertrophy (especially as to the condition of the median portion, whether a bar or a rounded or pedunculated lobe, and its elevation above the trigone (bas fond); the relative enlargement of the lateral lobes, etc. (b) The condition of the bladder wall; as to trabeculation, pouch formation, diverticula, inflammation, ulcers, calculi, etc. 3. With searchers (in absence of a cystoscope), which by rotary movements may determine quite accurately the presence of a middle lobe; and the relative size of the lateral lobes, as also the presence of trabeculations, pouches, etc. *Urinary examination*; especially with reference to the character of the infection, besides the ordinary tests.

Having then determined as accurately as possible the conditions present, a plan of action is mapped out: as to whether a Bottini operation or a prostatectomy be preferable, and if the former, what blade should be chosen, in

what directions should cuts be made, and what should be their length.

The following cases, including several forms of hypertrophy, give in detail the operation found applicable to each and the length of blade chosen. They demonstrate, I think, the *raison d'être* of the new combined cautery incisor, and its practical value. The work with this instrument being of recent date unfortunately prevents our showing the ultimate result obtainable, as several months must generally elapse before the full effects of the operation are secured.

CASE I.—J. N. M., age 71, had been suffering with urinary trouble for 4 or 5 years. During this time urination became steadily more difficult and more frequent until he now voids every  $1\frac{1}{2}$  hours, night and day.

*Examination* showed slight, but definite, enlargement of the prostate, which was much harder than normal, but not nodular. The cystoscope showed a small median transverse bar and a slight intravesical projection from the lateral lobes, but there was really very slight intravesical enlargement of the prostate. With a finger in the rectum a very slight increase in thickness over the normal was felt between it and the instrument in the prostatic urethra. The bladder, however, showed very definite effects of obstruction, viz., considerable trabeculation and pouch formation, a residual urine of 90 c. c., and a capacity of only 250 c. c. *Remark*: We evidently had to deal with the so-called small sclerotic prostate, furnishing moderate but definite obstruction and a bladder hypertrophied and somewhat contracted. The very slight enlargement and the small amount of prostatic tissue beneath the urethra made us afraid to use Freudenberg's instrument. A thorough prostatectomy would have been impossible, and as the case appeared to be in need of the Bottini operation, we persuaded the patient to wait until the arrival of our new incisor, so that we might use a smaller blade.

On May 31, 1901, a Bottini operation was performed with blade No. 2 of our instrument, which blade seemed to suit the case exactly. Three cuts were made: one posterior, 2 cm. long; and two lateral, the right  $2\frac{1}{2}$  cm., the left 3 cm., at right angles to the posterior [see diagram]. The instrument was used at a high heat; time, about 1 cm. to the minute; the operation done under control of a finger in the rectum. It was evident that a larger blade would probably have cut through the posterior capsule of the prostate.

The convalescence of the patient was as usual: difficult urination for the first few days and after that a gradual improvement.

The ultimate result was a complete relief of prostatic obstruction, micturition free, residual urine nil.

CASE II.—F. E. B., age 34, presented himself on June 30, 1901, complaining of bladder trouble. The patient had had nocturnal incontinence of urine up to the age of 14, and after that he always voided urine much too often. Seven years ago cystitis developed, and a calculus was discovered and removed by suprapubic cystotomy. The fistula did not

heal till eight months afterwards, and cystitis has persisted ever since. On admission he passed his urine about 6 times a day, generally with pain referred to the neck of the bladder.

*Examination.*—Patient was a rather neurotic young man. The urine is cloudy, acid and contained phosphates, pus cells and bacilli. The prostate examined by rectum was slightly enlarged, considerably indurated at the upper end of each lobe. The seminal vesicles were both indurated and closely bound to the upper end of the prostate. The fluid expressed from the prostate and the vesicles by massage shows pus cells. A rubber catheter was passed into the bladder, but met some constriction of the prostatic orifice. The patient had just voided, but a residual urine of 220 c. c. was found. The bladder capacity was 500 c. c. The cystoscope showed a marked trabeculation of the bladder wall, a considerable thickening of the interureteral bar, and behind it a deep pouch in which was a considerable collection of sand and small calculi, white in color.

Examination of the prostatic orifice revealed a definite thickening of the median portion in the form of a transverse bar, and behind it a fairly deep bas fond. There was no intravesical enlargement of the lateral lobes, but the entire prostatic orifice was irregular and showed numerous granulations.

*Remark.*—Although the patient was a young man, he had unquestionably an enlargement of the median portion of the prostate, which was causing considerable obstruction to urination, as shown by the trabeculation and pouch formations in the bladder and the presence of 220 c. c. residual urine. The prostate was undoubtedly chronically inflamed, but the enlargement while probably inflammatory in origin was unquestionably causing trouble, and in our opinion demanded a Bottini operation. The prostate, however, was so small that it was out of the question to use the ordinary Freudenbergs blade, so that patient was asked to wait until our instrument could be completed. In the meantime he was put upon bladder irrigations and given urotropin internally.

On September 13, 1901, examination showed considerable improvement in his cystitis, but the urine was still purulent. There was still 220 c. c. of residual urine present. Cystoscopic examination showed an improvement in the inflammation of the mucous membrane, and much to our surprise the considerable mass of small calculi which was previously found had disappeared. A very careful search was made with the cystoscope, but no calculous deposit could be found anywhere. There was still present the definite transverse median bar with a pouch behind it, and the bladder wall was still trabeculated. Accordingly the Bottini operation was performed, using blade No. 1 and making a single posterior cut through the median bar 2 cm. in length. There was some hemorrhage following this cut. After the operation the patient experienced considerable discomfort for a few days, but since then his condition has continued to improve.

It was intended to make three short cuts [see diagram] through the median bar with the small blade, but a burning out of some of the electrical

connections in the hospital after the first cut had been made prevented the others being made.

Now two months have elapsed since the operation, his condition is much improved and the residual has dropped to 150 c. c. Unless this disappears soon we shall make the two other cuts through the median bar as originally intended.

CASE III.—G. T. H., age 73, admitted Sept. 9, 1901, complaining of prostatic hypertrophy and catheterism. Urinary difficulty began soon after the age of 50, but did not get severe until about 1 year ago, when micturition became quite difficult, and the patient had to get up 2 or 3 times at night to urinate. About 10 months ago he had to resort to a catheter, which he has used ever since, being unable to void any urine naturally. He has had several attacks of inflammation of the bladder, and both testicles have been the seat of abscesses during the last 6 months. He now catheterizes himself regularly three times a day, and suffers very little discomfort, but the passage of the instrument is often quite difficult.

*Examination.*—Strong, healthy looking man, arteries slightly thickened, small nodules in both epididymes. Prostate markedly enlarged, about the size of a large orange, left lobe much larger than the right. The median furrow is deflected towards the right. The upper end of the prostate is hard to reach. The consistence is smooth, soft, not tender. Urine, acid 1014, not very cloudy, microscopically, numerous pus cells and bacilli.

Cystoscopic examination showed a very marked intravesical enlargement of the left lateral lobe, considerable enlargement of the median bar, and a lesser enlargement of the right lateral lobe, with a small rounded mass between the two lateral lobes in front. There was a very deep bas fond behind the prostate, and the bladder was very much trabeculated and inflamed. The blade of the Freudenbergs instrument would have been perfectly suitable for this case.

A Bottini operation was done under chloroform, blade No. 3 being chosen. This blade is of the same size as Freudenbergs'. The posterior cut was  $3\frac{1}{4}$  cm. long, right lateral cut  $3\frac{1}{4}$  cm. long, left lateral cut  $3\frac{1}{2}$  cm. long [see diagram]. The operation was done under the control of the finger in the rectum.

Hemorrhage moderate and patient in splendid condition at end of operation. 1000 c. c. submammary infusion of salt solution was given as a prophylactic against uremia. The patient made a rapid convalescence, required catheterization only 3 or 4 times after the operation, and very soon began to void urine naturally. His condition since then has steadily improved, until now the interval between urinations is every 2 hours during the day and longer at night. His general health has improved wonderfully, he has gained 12 lbs. in 2 months, and will apparently get a good result.

CASE IV.—E. W. S., age 63, admitted Sept. 13, 1901, complaining of enlarged prostate and catheterism. Urinary trouble began 4 years before with difficulty and frequency of urination, which at times had become so bad he had to use a catheter. For the past three months has had to use

catheter three times a day, and has not been able to pass any urine naturally. For the last four years the patient has suffered from diabetes mellitus, which has been somewhat controlled by dieting.

*Examination.*—Large, healthy looking man. The rectal examination showed a very large hypertrophied prostate, left lobe apparently larger than the right, consistence firm, but not nodular. Urine removed by catheter was acid, slightly cloudy, contained both albumin and sugar, and under the microscope showed pus cells and bacilli. After six days of diabetic diet there was barely a trace of it to be found. A rubber catheter entered the bladder with difficulty. The bladder tonicity was only moderately good, and the capacity about 500 c. c. The cystoscope showed a marked intravesical enlargement of the left lateral lobe, which projected into the bladder as a large rounded tumor, a moderate enlargement of the median portion, and a very slight enlargement of the right lateral lobe. Behind the prostate was a very deep bas fond in which the ureters could not be seen. The bladder was considerably trabeculated and inflamed.

Sept. 19, 1901. Bottini operation, under cocaine and morphia. On account of the considerable size of the prostate, blade No. 3 was used, and as the left lateral lobe was much larger than the right, a much longer incision was made on that side. The posterior median cut was  $3\frac{1}{2}$  cm. long, the left lateral  $3\frac{1}{2}$  cm., and the right lateral  $2\frac{1}{2}$  cm. [see diagram].

Time taken, 1 cm. to 1 minute. Instrument used at a white heat. There was very little hemorrhage following operation, and very little pain caused, the anesthetic being very efficient. Immediately after the operation the patient voided urine naturally, and has never been catheterized since. For the first few days there was considerable vesicle spasm.

On Oct. 2, 1901, 13 days after the operation, the following note was made: Patient now passes his urine about every 2 hours in a large stream and without pain. There is no dribbling. Residual urine 140 c. c. Urine, acid, quite purulent, pus cells and cocci present. Sugar is still present in considerable amount.

In a letter dated Nov. 5, 1901, the patient reports that he had not used a catheter since operation, that he urinates once during night and 4 times during the day, that his residual urine is less than 50 c. c., that micturition is free, and the vesical inflammation greatly improved.

CASE V.—J. P. A., age 71, referred to me by Dr. Finney on Sept. 28, 1901. The patient gave a very long urinary history, which began with difficulty in micturition 11 years ago, when a stone was found and removed by a surgeon through a suprapubic opening. For two years following this he had a suprapubic fistula, which was finally cured by his taking up catheter life in 1895. Castration was then done by another surgeon, and several weeks later another suprapubic to remove another stone. During the next year the stones reformed and were crushed by a third surgeon. After that he was free from pain for a while, but had to use a

catheter. Stones soon appeared again, and during the next 12 months 4 separate litholapaxies were done. In 1897 still another surgeon did a suprapubic operation and removed stones, and at the same time removed by means of the Rongeur forceps a moderate-sized median lobe which was still present (despite the castration). After this operation, for the first time the patient was able to go without the use of the catheter, but micturition has been too frequent.

*Status Presens.*—Patient on admission complained of irritation of the bladder. He urinated every 2 hours during the day and twice during the night, but had no pain or discomfort during urination. Rectal examination: The outlines of the prostate were easily made out, and a little larger than normal. In the median line the prostate presented a slight but distinctly abnormal rounded mass. The lateral lobes were apparently much atrophied and sloped away from the central mass, which replaced the median groove and notch. The whole diameter of the prostate was half as large again as normal, the consistence of the lateral lobes soft and flabby. Urine, acid, 1022, containing pus cells, bacilli and cocci.

Cystoscopic examination: Rubber catheter met an obstruction about 7 inches from the meatus, but a silk one passed with ease. Patient had just voided, but 320 c. c. of residual urine was found in the bladder. Cystoscope showed two fairly large stones in a pouch behind a considerably hypertrophied interureteral bar. The mucous membrane of the bladder was much inflamed, but not markedly trabeculated, and there were no ulcers to be seen. Examination of the prostatic orifice showed a small but definite transverse median bar behind which there was a shallow bas fond. There was no intravesical enlargement of the lateral lobes to be seen, and there were no sulci between the lateral lobes above, nor between them and the median bar.

*Remark.*—The castration had removed the enlargements of the lateral lobes, but the median lobe persisted after that. The removal of this through a suprapubic opening allowed the patient to urinate without the use of a catheter, but there still remained a definite transverse bar at the median portion (the base of the middle lobe) which continued to act as an obstruction, 320 c. c. of urine remaining in the bladder after micturition. It was evident that after litholapaxy a Bottini operation should be done to remove this obstructing bar, but the amount of tissue felt beneath the instrument in the urethra was so slight that it was decided to use the smallest blade of the incisor.

On Oct. 17, 1901, under cocaine and morphia, litholapaxy was done, and followed by a Bottini operation. The crushing and evacuation of the stone was easily accomplished after placing the patient in the Trendelenburg position. The largest stone was one inch in diameter. All fragments were sufficiently crushed at the first introduction of the lithotrite to be removed by evacuation afterwards. After all debris had been removed, the bladder was washed clean, cocaine again inserted into the bladder and urethra, washed out after three minutes, and a Bottini operation performed. For this purpose blade No. 1, which

in this case was 8 mm. high, was used. Three cuts were made through the median bar, each  $1\frac{1}{2}$  cm. long, one cut being in the median line posteriorly, the other two cuts were made at angles of about  $50^\circ$  to the median cut [see diagram]. The operation was done with the forefinger of the right hand in the rectum pushing the prostatic bar into the angle of the beak of the instrument. This was done because it was feared that the length of the beak in the bladder would so depress the trigone and bar of the prostate that the knife would not penetrate it for its full depth.

The patient stood the operation well; anesthesia quite good; very little hemorrhage. He was unable to void his urine afterwards, and had to be catheterized three times in the next 24 hours. When seen a week after the operation he was voiding urine quite freely and the residual had dropped from 320 to 150 c. c. and he was already feeling greatly improved. He attended his office on the fourth day after the operation.

Condition one month after operation: Steady improvement, residual now 125 c. c., sometimes more. Bladder still large and weak in tone, but condition improving.

Nov. 21, 1901. Bladder capacity 400 c. c., tonicity considerably improved; residual, however, 175 c. c.

CASE VI.—J. A. B., age 70, admitted Oct. 18, 1901, complaining of enlarged prostate and catheterism. His urinary trouble began ten years before with difficulty and frequency, which soon became so aggravated that he began the use of a catheter, which he has used continuously up to this time. For the past 7 years he had been unable to void any urine naturally, and when admitted passed a catheter about every two hours during the day and about every three hours during the night, using a very large rubber catheter. Examination showed a very large, hard prostate and a considerable dilatation and lengthening of the urethra just in front of the prostate. The cystoscope revealed a moderate-sized stone in a pouch behind the prostate, and a very much inflamed and trabeculated bladder. There was present a considerable intravesical outgrowth of the prostate, which appeared as a collar-shaped enlargement, both lobes and the median portion being hypertrophied, the left projecting farthest into bladder. Behind the median bar was a deep pouch. The bladder capacity was rather small. The urine, which was obtained always by catheter, contained many red blood-corpuscles, pus cells and bacilli, and was acid in reaction.

On Oct. 23, 1901, litholapaxy was done under chloroform. The operation was begun under cocaine, but chloroform had to be used on account of pain. The largest diameter of stone grasped by the instrument was 2 cm. The crushing and evacuation were both difficult on account of the great hemorrhage caused and the trabeculated condition of the bladder. Patient stood the operation well and was very much more comfortable afterwards, but still required catheterization.

On Oct. 26, 1901, a Bottini operation was done under cocaine  $\frac{4}{8}$  and a hypodermic of  $\frac{1}{4}$  gr. of morphia. Blade

No. 3 was chosen as the proper size for all of the cuts, of which three were made, one posterior through the median bar  $2\frac{1}{2}$  cm. long, a right lateral  $2\frac{1}{2}$  cm. long, left lateral 3 cm. [see diagram]. The duration of cuts was about 1 cm. to 1 min. and a high heat was used on the blade. There was very little hemorrhage following the operation, and immediately afterwards the patient voided urine.

Patient made a rapid convalescence, voiding his urine freely immediately after the operation and never after required catheterization, although he had led a catheter-life for 7 years.

On Nov. 7, 1901, 12 days after the operation, he reported that he was rapidly improving, that he passed his urine once every three hours without any straining and was free from pain. A catheter passed 4 weeks after operation finds no residual urine, and the cystitis considerably improved.

CASE VII.—J. M. D., age 73, admitted Oct., 1901, complaining of hypertrophy of the prostate and catheterism. Urinary trouble began about 7 years ago with difficulty of urination. A little later retention of urine became complete. He then began to use a catheter, and has had to use it ever since, never being able to pass any urine. He has remained in fairly good health, has had very little inflammation of the bladder, and now has to pass a catheter about every 4 hours, twice during night. Increasing difficulty in introducing the instrument of late has driven him to the operation.

Examination.—Large, healthy looking man, arteries slightly thickened, heart and lungs apparently normal. Small hydrocele of right side. Prostate very much enlarged, about the size of a moderate-sized orange, lateral lobes about equally enlarged, contour round, smooth, consistence hard. Seminal vesicles indurated, but not nodular. A rubber catheter met obstruction  $9\frac{1}{2}$  inches from meatus. The bladder capacity was 400 c. c., tonicity rather poor. Urine acid, slightly cloudy, and contained pus cells and bacilli. The cystoscope showed a very markedly trabeculated bladder with numerous small pouches. Behind the prostate was a very deep bas fond in which the ureters could not be seen. There was considerable inflammation of the mucous membrane. Both lateral lobes and the median portion were very much enlarged, presenting a large collar-shaped intravesical hypertrophy around the urethral orifice, which projected well out into the bladder cavity. Growing from the upper portion of the lateral lobes, especially the left, were numerous small villi, which floated in the fluid but caused no hemorrhage. There was no ulceration of the surface of the prostate.

Oct. 28, 1901. Bottini operation, cocaine and morphia. Blade No. 3 was chosen. Four cuts were made, one in the median line posteriorly across the median bar  $3\frac{1}{2}$  cm. long, one right lateral cut 3 cm. long. Through the left lobe 2 cuts were made, one lower oblique at an angle of about  $75^\circ$  to the median posterior cut  $3\frac{1}{2}$  cm. long, and an upper

oblique cut at an angle of about  $130^\circ$  to the posterior median cut also  $3\frac{1}{4}$  cm. long. The direction of these cuts is best shown in the accompanying diagram. Patient stood operation well. There was very little hemorrhage, and anesthesia was quite good. Time occupied was

about 1 cm. to 1 min. For the first 24 hours after operation the patient voided urine with considerable ease, after that it became more difficult, the bladder becoming irritable and catheter had to be used for six days. After that patient began to void without the use of a catheter.

Condition three weeks after operation: Patient voids about every hour, but sometimes  $2\frac{1}{2}$  hours elapse between urinations. The vesical inflammation is improving, and its capacity increasing gradually. The catheter on which he depended for seven years has not had to be used for two weeks.

On Nov. 21, 230 c. c. of urine was voided at a time with an interval of two and a half hours. Urination fairly free, stream large. Residual urine, 10 c. c.

Dec. 13. Patient voids urine about 6 times in 24 hours, in amounts varying from 150 to 210 c. c.

CASE VIII.—S. M. A., age 56, admitted Oct. 28, 1901, complaining of frequency of urination. His prostatic trouble began  $2\frac{1}{2}$  years before with difficulty of urination. Since then micturition had become gradually more frequent and difficult, and one year before he had begun the occasional use of a catheter. On admission he complained of a dull pain at the beginning of urination, which occurred every 2 or 3 hours during night and day. He had suffered considerably with inflammation of the bladder.

On examination patient was found to be a man in fairly good health. The prostate on rectal examination was found to be slightly enlarged, soft in consistence, contour smooth and round, and both lobes of about the same size. The seminal vesicles were not indurated. The urine was cloudy, specific gravity 1017, pus cells and bacilli were present in considerable number. A rubber catheter passed with some difficulty, owing to obstruction in prostatic urethra. Residual urine 185 c. c. (another examination 3 weeks later showed a residual of 375 c. c.). The bladder capacity was between 500 and 600 c. c.; tonicity fair. Cystoscope showed a small median bar which joined, without intervening sulci, with two very slight intravesical enlargements of the lateral lobes. Behind this median bar was a definite, but not very deep, bas fond in which the ureters lay, rather close up to the prostate. The interureteral bar was considerably enlarged and behind it was a rather deep pouch. The posterior wall of the bladder was very greatly trabeculated, and between some of these trabeculae small round and oval openings were seen which connected with extravascular pouches. About 1 inch behind the left ureter a very considerable diverticulum with a large round opening into the bladder was seen, and the cystoscope was introduced into this for some distance, and a cystoscopic examination of the diverticulum made. With a finger in the rectum and the cystoscope in the urethra

the amount of prostatic tissue between them was found to be very little thicker than normal; more than in Cases II and V, but much less than usual in prostatic enlargements.

The rectal examination and cystoscopic examination both showed only a slight enlargement of the prostate, but the considerable residual urine and the marked evidences of obstruction as shown by the trabeculation and pouch formation in the bladder wall made it evident that there was considerable hindrance to urination. The prostate was so small that prostatectomy would have been very difficult, although the patient was in splendid shape for any operation, and the ordinary Freudenberg instrument would undoubtedly have been dangerous to use on account of the danger of penetrating the capsule of the prostate. Blade No. 2 of our instrument appeared to be the proper size to be used with cuts not longer than 2 cm.

On Nov. 20, 1901, a Bottini operation was performed under cocaine and morphia. Blade No. 2 was used in accordance with the cystoscopic and rectal examinations as stated above;



5 cuts were made as shown in the diagram. One median-posterior and two oblique on each side, one at an angle of  $75^\circ$  to the median posterior, and the other at an angle of  $120^\circ$ . Each cut was made 2 cm.

in length. Patient stood operation well. There was very little hemorrhage from the cautery cuts. The catheter was not required after the operation.

On the day following the operation there was a temporary suppression of urine, which was relieved by subcutaneous infusions and digitalis.

Dec. 13. Patient has done well. Urine voided freely, often 300 c. c. at a time. Residual urine 0. Cystitis improving. Result excellent.

*Reviewing the eight cases reported in full, we find four cases (III, IV, VI, VII) in which blade No. 3 was used. All of these were fairly large hypertrophies of both lateral lobes and median portion, and were suitable cases for Freudenberg's instrument.*

In two cases (I and VIII) blade No. 2 was used. In both of these the prostate was very slightly larger than normal, as shown by rectal, instrumental and cystoscopic examinations, but in both of these cases there was marked evidence of obstruction and the cases urgently needed operation. In both cases, however, incisions made with Freudenberg's instrument would probably have penetrated beyond the confines of the prostate, but the operations were performed safely with blade No. 2 of our instrument.

In two cases (II and V) blade No. 1 was used. In both the obstruction was caused by a very small median bar, associated with complete atrophy of the lateral lobes (after castration) in one case and lobes of normal size in the other. In these cases the amount of tissue beneath the instrument was so small that we feared to use even blade No. 2. In another case (not here reported) the enlargement consisted

in two very large lateral lobes, associated with a complete absence of median bar, the urethra skirting the posterior surface of the prostate and the amount of tissue between the rectum and a sound in the prostatic urethra being very small. In this case we used blade No. 3 for the lateral lobes and blade No. 1 for the posterior cut.

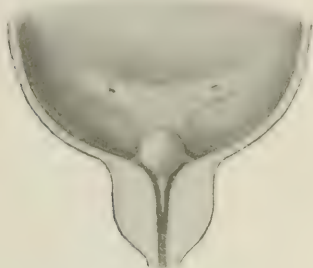


FIG. 8.

I have not as yet used blade No. 4, and hardly think it will often be necessary except to attack a single very great hypertrophy of one lateral lobe. I have, however, seen several tremendous general hypertrophies in which it would have been necessary.

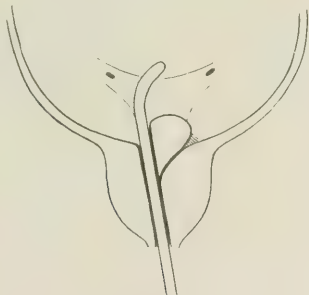


FIG. 9.

As to the efficacy of the Bottini operation, of which I was myself at first very skeptical, my experience (now of 41 operations) forces me to testify decidedly in its favor.

In 41 cases I have had three deaths, all men in very bad condition before operation, and two with pyonephrosis. Fifteen patients were over seventy years of age, three over 80, and among these there have been no deaths, and all but one have been cured of the prostatic obstruction. Of thirteen patients who had to use the catheter, there is only one who still requires it, and this one is considerably improved. Some of my cases are of too recent date to show the ultimate results, and these I will reserve for a later publication. I am still, however, of the opinion (from an experience of 15

prostatectomies) that in certain cases, *e. g.*, men between 45 and 60, in good condition, and with easily enucleable enlargements, a complete prostatectomy is a very safe operation, and certain as to lasting results, though I must say the effects of the Bottini operation seem to be also permanent. Time, careful study of cases (especially with the aid of the cysto-

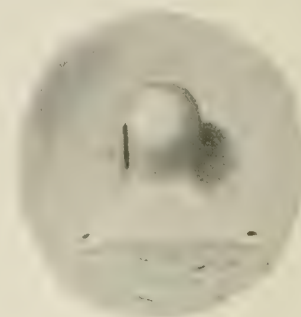


FIG. 10.

scope) and long-continued observation after operation can alone determine the applicability and the limitations of the principal operations for the treatment of prostatic hypertrophy.

In closing the paper I cannot too strongly urge that the



FIG. 11.

Bottini operation should be performed in accordance with the character of the prostatic obstruction as found by exhaustive examination as previously outlined. There is no doubt but that a perfunctory performance of the operation with one blade for all cases, and one cut directed posteriorly and one laterally on each side, while perfectly satisfactory in a large number of cases, is insufficient in some and dangerous in others.

As shown by the writer in another paper,<sup>1</sup> when a decided median lobe (more or less pedunculated) is present, the ordinary operation is entirely inadequate, as the posterior

<sup>1</sup> Monatsberichte für Urologie, Jan., 1901.

cut will generally pass to one side of the median lobe and leave it to continue its obstructive work [see Figs. 8, 9, 10].<sup>2</sup> If, however, the cuts be so made as to pass obliquely across the base on each side of this projecting lobe,<sup>3</sup> I have shown that this lobe may be dropped back out of the way and a rapid atrophy induced by thus cutting off most of its blood-supply [as in diagrams, Figs. 11, 12, 13]. This has been abundantly proved in five cases, some of which were entirely unaffected by the usual three incisions and the prostatic obstruction immediately removed by the incisions described above.

The cases outlined above serve to show the selection that may be made in some forms of hypertrophy as to the size of blade to use, and as to the length of incisions, their

<sup>2</sup>To be more explicit: Fig. 8, shows the Y shaped urethra which is present in these middle lobe cases, and Fig. 9 shows how a metal instrument that has been introduced into the bladder will pass to one side of the middle lobe, and not remain on top of it. Fig. 10 illustrates a case in which I performed the usual Bottini operation with no result, and a subsequent suprapubic cystotomy showed the posterior cut on one side of the middle lobe as shown in Fig. 10.

<sup>3</sup>This is accomplished by the following manoeuvres: Introduce incisor, draw beak up against anterior portion of the prostatic orifice, rotate instrument 180° (hugging the prostatic orifice all the while.) This will bring beak into sulcus to one side of middle lobe. Carry the rotation 45° further and beak will lie obliquely across the base of the middle lobe, ready for the first cut, Fig. 11. By reversing these movements the cut on other side of middle lobe may be similarly performed, and then the two lateral cuts made, Fig. 12. The result is shown in Fig. 13, a diagram from an autopsy specimen.

number and direction. No two cases are alike, and each should be a study unto itself.

As a rule, the usual three incisions—one posterior and two lateral—are entirely sufficient for most cases, especially those of moderate hypertrophy, where with more incisions the danger of causing a slough, too large to be passed per urethram, is considerable. The same rule applies to middle

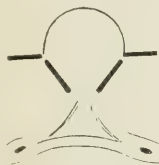


FIG. 12.

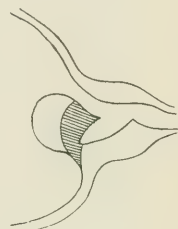


FIG. 13.

lobe cases: unless the median enlargement is considerable the single posterior incision should be preferred as free from all chance of completely amputating the middle lobe, and leaving it to act as a foreign body in the bladder. In the choice as to the length of incisions and the size of blade to use, there is considerable latitude, and it should always be based on a careful study of the conditions present and controlled by rectal touch.

## THE DISTRIBUTION OF ANOPHELES IN THE VICINITY OF BALTIMORE.<sup>1</sup>

BY LEONARD K. HIRSHBERG AND GUSTAVUS C. DOHME,

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In the spring of 1901, at the suggestion of Doctor Thayer, a study of the distribution of *Anopheles* larvæ infesting the ponds and streams in and around the city of Baltimore was undertaken. Thayer and Lazear (1) had already found adult *Anopheles* at Sparrows' Point, a suburb of Baltimore, in 1899. The larvæ, however, had never been found.

Our search for the larvæ ultimately extended over the whole of the city and nearly all of its suburbs and neighboring villages. These included Sparrows' Point, Chesapeake Mills, River View, Orangeville, Gardenville, Dickeyville, Windsor Heights, Roland Park, Calverton Heights, Brooklyn, Middle River and Back River.

Along these latter rivers, which are tributaries of the Chesapeake Bay, there are scattered a number of club houses, hotels and pleasure shores, where city people go to fish, shoot and enjoy an outing during the summer season.

These places, therefore, are usually rather densely populated from June until October.

It was very interesting to note that a very definite line could be drawn across the city, above and to the west of which the larvæ of *Anopheles maculipennis* were rarely found, and below and to the eastward of which few *Anopheles punctipennis* were ever taken.

The larvæ of *Anopheles punctipennis* did not appear until about the middle of July, while the first *Anopheles maculipennis* were obtained on June 20.

Wherever or whenever *Anopheles* larvæ were taken the approximate number of them per cubic metre, if possible, was always estimated for the time and the place. This method, of course, applied to a given body of water, gives no notion as to their number and distribution. For, in the backwater of the Chesapeake Bay, about one hundred and fifty larvæ of *Anopheles maculipennis* were found in one cubic metre, and not another larval form was found within a radius of one mile.

<sup>1</sup>Read at the meeting of the Johns Hopkins Medical Society, Dec. 16, 1901.

The larvæ were captured throughout the summer until October 22 in the backwater of the Chesapeake Bay and Patapsco river seventy times; twelve times in stagnant pools; in slowly flowing, almost quiet brooks and pools twenty times. In marshy ground with very small scattered patches of water, larvæ were taken five times. One *Anopheles maculipennis* was found in a rotting log filled with rain water.

The common bullrush or cattail, *Typha latifolia*, was a shelter beneath which *Anopheles maculipennis* was nearly always found. Neither species of *Anopheles* was ever taken in artificial receptacles such as boxes, basins, kitchen utensils, flower-pots or any such vessel which might contain water, although Drs. Cassidy and Bayne of Roland Park found *Anopheles punctipennis* in rain barrels.

Larvæ of *Culex* were found in the same bodies of water with *Anopheles* much more frequently than the results of other investigators would lead one to suppose. The larvæ of both *Anopheles* and *Culex* occurred together in all but ten cases above, only a few *Culex* in fifteen instances.

In eighty cases larvæ were found alive and thriving in the same places as fish. In several cases sunfish, perch, trout and gudgeons could be seen below the larvæ waiting for food of a larger sort. Twice it was our fortune to find boys fishing near the rushes where the larvæ were captured, and a snap-shot was taken by Dr. Eldred, of Sparrows' Point, who accompanied us on this excursion.

After several days of heavy rain, the young forms of *Anopheles* larvæ became very numerous. It was also noted that the water about the margins of petiolized pools contained larvæ when they were examined several days after a period of rainfall. In such cases the petroleum had collected toward the middle of the pool and appeared to be diminished in amount.

Although under natural conditions the larvæ seem to thrive very well in the presence of fish in some natural ponds and rivers, when we, however, attempted to breed larvæ in an aquarium in order to test this fact, it was quickly found that the larvæ were all eaten by the fish. This was so even when sunfish and perch were placed in the aquarium. Sunfish and perch only were used for this experiment. Both species devoured the larvæ, even when well supplied with other food.

Of forty *Anopheles* imagines captured, ten of which were *Anopheles punctipennis*, and thirty *Anopheles maculipennis*, not one contained sporozoites or zygotes. Only eight of these, all *maculipennis*, were captured inside a house, the persons in the house being free from malaria.

The larvæ were usually collected in small bottles or fruit jars with loose screw tin tops, through which sufficient air passed to keep the larvæ alive. In transporting the larger and more nearly mature forms we often killed them by jolting during transportation. The smaller forms rarely died in this way. Nuttall, Cobbett and Strangeways-Pigg (2) call attention to this fact.

An ordinary white porcelain saucer was employed for dipping the larvæ from their pools, and in order to avoid

transferring an unnecessary amount of water into the bottles with the larvæ, a long pipette with a rubber bulb attached was used to take up the larvæ from the saucer, as recommended by the above writers (3).

When it became necessary to wade out farther than boots or our bare feet and legs could take us, the saucer was placed in the bottom of a long-handled, shallow crab net. A dip could be carefully made with this and any larvæ easily detected over the white surface of the saucer.

The color of the larvæ was usually black, but this was not invariably the case. In four different pools with clear shallow water over a fine sandy bottom they were almost the color of crayfish. In two other sluggish streams with a fair amount of vegetation growing in and around the margins, the larvæ showed a distinct greenish tint, even more noticeable after being taken from the stream. The green color did not seem to be due to food within the digestive tract.

Occasionally, in a mass of larvæ, about one-quarter of them showed a quadrangular white area in the mid-dorsal region of the thorax and the third abdominal segment. This was only observed in the *Anopheles punctipennis* series. Dr. Cassidy first called attention to this.

The larvæ are most commonly found around or near the margins of pools, etc. If there are islands of algae, *Typha latifolia* or other vegetation in the middle of the water, larvæ are frequently at the bottom, in the mud which accumulates about or near the roots of the rushes.

Although, as has often been stated, any passing breezes blow the larvæ towards the margins of the ponds, the fact that they are on the windward edge of the bank, as well as on the leeward side, and are also arranged in a radiating manner around the sides of artificial receptacles in which they are kept in the laboratory, cannot be accounted for by supposing that the wind causes them to take such positions.

By carefully observing the larvæ after they have been disturbed, it can be seen that their movements are made so rapidly and always tail first that they are not brought to a halt until the impact of their tails against the sides of the vessel. When all is quiet again, they may be seen ranged about the sides, radiating towards the centre of the vessel, head first. The methods of differentiating larvæ of *Anopheles* from the larvæ of *Culex* are now so well known that any detailed information is quite unnecessary. It may be obtained from the book of Dr. L. O. Howard (4) or the articles of Nuttall and Shipley (5).

About the average number of *Anopheles* larvæ brought to the imago stage was five in every twenty, or 25 per cent. The average length of the larvæ captured was 2.9 mm., although they ranged in size from 1 mm. to 9.2 mm.

The average time for the larvæ to become pupæ was twenty-two days in July and August with an average temperature of 28.5°, and taken during the day.

Two days was our average time for the pupæ to cast their shells and become imagoes. It was very difficult to keep the adult *Anopheles* in confinement even with the most careful attention. One week was the average duration life of the



Chesapeake Mills.



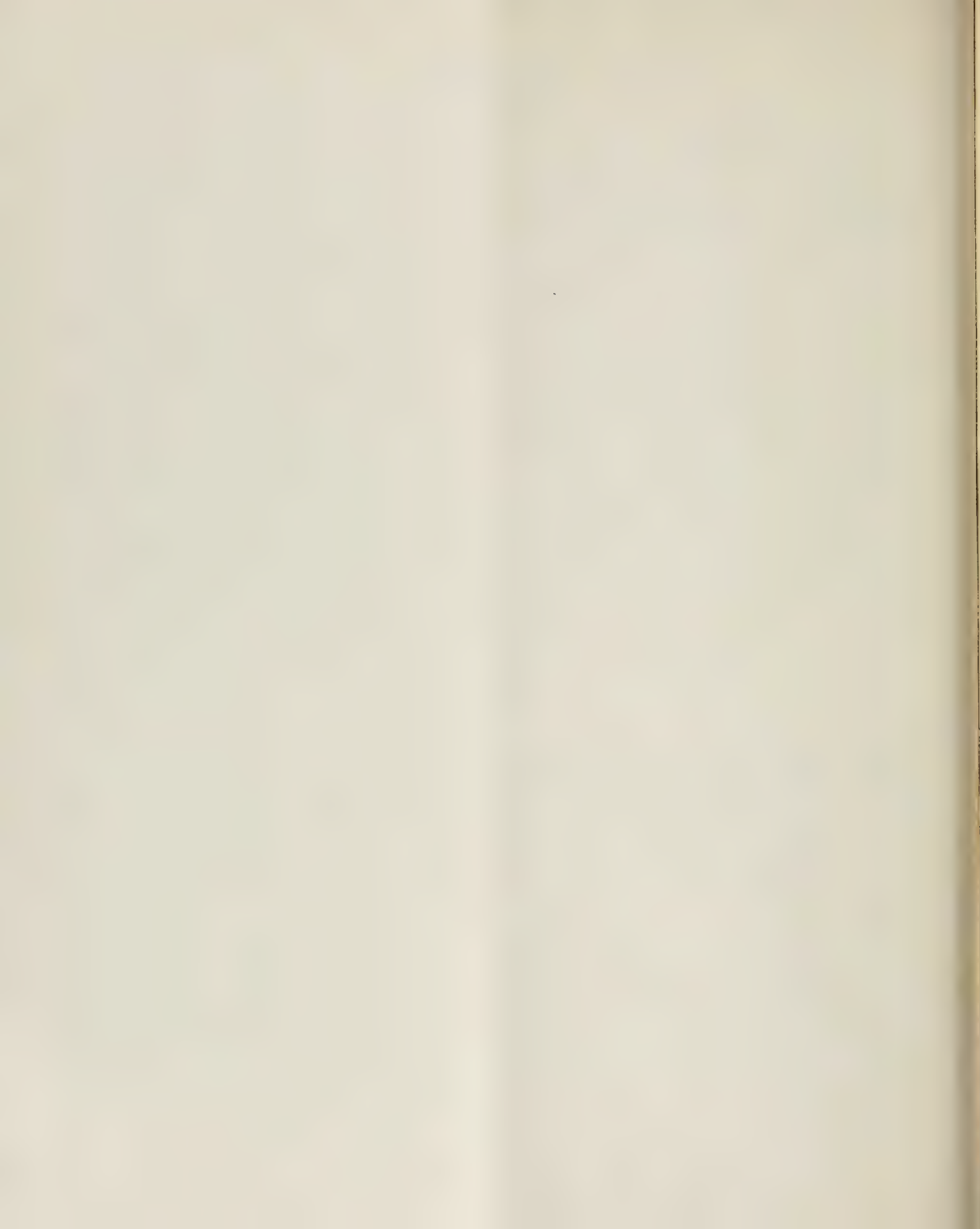
Sparrows Point.



Point midway between Sparrows Point and Chesapeake Mills.



Inlet of Chesapeake Bay at Sparrows Point. Fishing among the cat-tall bullrushes.



adults during July and August, and it seemed easier to keep *Anopheles maculipennis* alive in the cages than *Anopheles punctipennis*. One *Anopheles maculipennis* was kept seventeen days, the longest period of any adult in our series during these warm months. Later in the fall as the average daily temperature fell, it was very easy to keep the adults for sixty days with careful attention.

The larvæ were always kept in a large, well-lighted and ventilated laboratory having windows facing east, north and west. The receptacles which contained the larvæ were of glass (and either circular, cylindrical or globular in shape). They ranged from ten to thirty centimetres in diameter and from five to ten centimetres in depth. Similar vessels were also used for holding the food. As the larvæ increased in size they were placed in larger glass jars and over these was placed fine gauze mosquito netting to prevent the egress of mosquitoes and the ingress of house-flies. Two vessels were kept in a cage made of wire screening of closely woven meshwork. This box was thirty-four centimetres square and had been previously used for caging mosquitoes by Thayer and Lazear.

Experiments relating to the food of the larvæ were tried with the following results. Thus, as suggested by Manson (6), rice was added to the water in two instances, and the rapid growth of bacteria which followed completely cut off the supply of air for the larvæ by the formation of a thick, gelatinous film of zooglee over the surface of the breeding jars. The larvæ were all killed.

Cultures of *B. lactis aerogenes*, *B. violaceus*, *B. prodigiosus*, *Pencilium* spores, *B. subtilis* all multiplied rapidly, so rapidly, indeed, that the larvæ could not use them as food, but were in turn killed by them or by their products formed from them.

The larvæ thrived best upon diatoms, *Spirogyra* and other algæ and protozoa, which are usually found in the natural habitat of the larvæ, and can be collected along with them. It was found that supplies of algæ could always be kept in sufficient quantities to last for days if they were cultivated and thrown in aquaria containing no mosquito larvæ. This was very convenient, inasmuch as it became necessary to change the water frequently in warm weather and consequently required considerable numbers of them to furnish food for our embryo mosquitoes.

When the imago left its pupal shell, immediate provision was made to keep it supplied with necessary food. If ripe fruit could not be at once obtained, one of the writers permitted the females to feed from his blood until fresh bananas or oranges could be furnished.

Pieces of freshly cut banana or orange were kept in the cages when adults were present, and occasionally the females were allowed to have some human blood. The females seemed to bite as well during the day as during the night.

Six *Anopheles maculipennis* were permitted to bite the blood of patients suffering from the æstivo-autumnal form of malarial fever, in whom crescents had already been demonstrated. The method employed was as follows: One of

the newly hatched mosquitoes was captured by placing a wide-mouth test tube over the insect while at rest, in the manner advised by Thayer (7). The mosquito would rise to the top of the tube after a time, and a cotton plug was then quickly placed over the mouth of the tube. The lobe of the patient's ear was then carefully cleansed with alcohol and allowed to dry. The cotton in the mouth of the tube was then carefully replaced by the lobe of the ear. This was best done beneath the bed clothing, although it was also successfully done in one instance in the open light of day. The female *Anopheles* bores her proboscis into the lobe of the ear practically without the knowledge of the patient. Once this occurred without disturbing the patient, a sleeping boy of sixteen years. In only one instance was any complaint made, and this in the case of an hysterical female.

After *Anopheles* had bitten the patient, it was placed in an incubator at a temperature of thirty degrees centigrade and allowed to remain there for five, six, seven or eight days.

In none of the six cases were we able to demonstrate zygotes or sporozoites in the stomach wall, body cavity or salivary glands. Fresh preparations were always employed and the usual method (8) for dissecting the mosquitoes was carried out. A Leitz one-twelfth immersion lens was used in the microscopic work. The mosquitoes when examined were placed in normal saline solution on an ordinary slide.

The adult *Anopheles* was often caught flying near the pools where larvæ were found. This was observed only about dusk. During the day, *Anopheles* was rarely found and then usually at rest unless disturbed. The only imagines caught inside of dwellings were females, swollen with the blood they had imbibed. They were always sluggish when disturbed and easily captured on the wing. *Anopheles punctipennis* was observed to hatch out often during the day.

In all, *Anopheles* were collected one hundred and six times in forty-six different places; *Anopheles* and *Culex* were found together ninety-six times. In fifteen cases *Culex* were few, only one, two or several more being present. Fish occurred in the same streams as the larvæ eighty times. These cases all occurred at Sparrows' Point.

The inlets from the river and bay at Sparrows' Point have their borders filled with *Typha latifolia*. Among these rushes, hidden from their enemies, the larvæ of *Anopheles maculipennis* were found continuously from June the twentieth until October the twenty-second.

At Chesapeake Mills, about a mile from Sparrows' Point, stagnant pools and salty backwaters are likewise alive with the same larvæ. A chain of *Anopheles*-infested pools follows a line parallel with the tracks of the Pennsylvania railroad from Sparrows' Point to Chesapeake Mills. One other pool between Baltimore and Chesapeake Mills contained them also.

A clear, slowly-flowing brook near Towson yielded large numbers of *Anopheles punctipennis*. Other small pools of water in neighboring places also contained them. No adult were captured in houses but several males were taken from the thick, low foliage near the water.

A small run or brook near Govanstown, on the York Road, which flows over a limestone bed showed larvæ of *Anopheles punctipennis* in the water of gullies and holes left by the receding stream after a period of dry weather.

At Roland Park the larvæ were found in two stagnant pools thickly covered in places by a green scum (*Lemna* ?) (3). One of these pools contained myriads of *Culex* larvæ and was situated alongside the principal thoroughfare. *Anopheles* larvæ were also found by Drs. Cassidy and Bayne (who carefully worked over the region around Roland Park) in old receptacles containing water, in a rain barrel and in various pools and marshes. We found them in a stream not far from the railroad and also in two very clear ponds near a golf course and in the Country Club grounds.

A stream running through Windsor Heights and Walbrook contained a few *Anopheles punctipennis*, but no *Culex*.

At Calverton, *Anopheles punctipennis* was found only once in a stream of dirty water.

Brooklyn, Anne Arundel County, yielded several small streams with *Anopheles maculipennis* and a great number of *Culex*.

The Herring Run, Jones Falls, the Gunpowder River, Bush River, Middle River and Back River, were each carefully searched by one of us without success, and the entire surrounding country was threshed out as mentioned above.

It might be of interest to know that some cattle brought from Queen Anne's County on one of the excursion boats were observed to have mosquitoes hovering about them when taken aboard about eight o'clock one evening at Queens-town. There was one *Anopheles* among them, the species of which was not determined.

In conclusion, then, we may say:

First. With regard to the general distribution, that the breeding places of *Anopheles* are found in the suburbs to the north, east, south and west of the city. But that *Anopheles punctipennis* breeds in the higher sections of the neighboring country, namely, to the north and west; while *Anopheles maculipennis* is to be found where the country is lower and the water salty, namely, to the east and south.

Second. Since the bite of the mosquito is now known to be the source of infection in malarial diseases, the question of prophylaxis is largely one of exterminating these insects. This can only be accomplished by destroying the pools

already infested with *Anopheles* and by preventing the formation of others. A moment's reflection will scarcely be necessary to show the difficulty of carrying out what is now at least, apparently a hopeless task. Innumerable pools of stagnant water fed by the ebb and flow of the tide of the Patapsco, in the low marshy country along the river front especially in the neighborhood of Sparrows' Point and intermediate places, offer an almost insuperable obstacle to the proper drainage of the infected districts. Nor does the filling in of the marshy places bordering on sluggish streams in other places present a more feasible solution to this difficult problem.

Third. In view of these facts it should be emphasized that other means must be adopted if the disease is to be stamped out. As Manson has well said: "In proportion as the liability to mosquito bite is diminished, exactly in the same proportion is the liability to infection reduced." Hence of special importance is the careful screening of doors and windows by wire gauze or mosquito netting as suggested by Celli. Where this cannot be done, fitting the beds with netting will offer security, inasmuch as most *Anopheles* bite at night. Again, persons already infected should be protected by screens to prevent infection of healthy mosquitoes and thus spread the disease broadcast; inasmuch as a patient having been infected in one place may carry it to another and infect the mosquitoes there.

Finally, cases of malarial infection should be reported to the city Board of Health just as are the contagious diseases; and thus enable precautions against the spread of malaria to be carried out under the proper supervision.

We again wish to express our thanks to Dr. Thayer for his kind suggestions and also to Drs. Cassidy and Bayne, of Roland Park, and Dr. Eldred, of Sparrows' Point, for much assistance.

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## A NEW METHOD FOR THE DEMONSTRATION OF THE FRAMEWORK OF ORGANS.

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Although in recent years much interest has been taken in the study of the connective tissues, it is nevertheless true that our knowledge of these important structures has

grown only by small increments. The results apparently have neither been commensurate with the importance of the questions involved nor the interest that has been taken

in them. Many anatomists believe, moreover, that the mesoblastic tissues as a whole have scarcely received the attention they deserved, in comparison with the relatively greater amount of work that has been done in their ecto- and endodermic neighbors. It seems probable, too, that the simple connective tissues may have a more important rôle in the general economy than the simple sustentacular function usually assigned to them. The probability of their association with certain physico-chemical phenomena of secretion, their arrangement to provide for certain degrees of elasticity, to meet the stress and strain of organs, their importance pathologically, are all suggestive facts which support this view. For example, recent work on the behavior of solutions and osmotic phenomena suggests the possibility that the basement membranes of glandular acini as well as the cytoplasm of the secreting cells may possess the property of semi-permeability. Now, when we consider the great results that have followed the application of the principles of physical chemistry to morphological and physiological problems, it does not seem improbable that we shall be able to revert to the older theories of secretion and show that part of these phenomena are merely expressions of simple physico-chemical laws, rather than the result of the activities of cells under the influence of secreto-motor nerves.

Many methods have, up to this time, been devised to show the framework of organs and the connective tissues of the body, among which may be mentioned those of teasing, selective staining, precipitation, maceration, and digestion. All of these methods have been, and indeed still are, valuable in the study of the connective-tissue framework of various organs and tissues, but there is little doubt that the most fruitful results have followed the use of the several destructive methods, of which tryptic digestion is perhaps the most effective. Ewald and Kühne<sup>1</sup> were the first to use this method in separating elastic fibres from the reticulated tissue of the lymph glands which they supposed were composed of collagenous fibrils. Mall,<sup>2</sup> in his study of the reticulated tissues undoubtedly made the greatest improvement in our technique by digesting frozen sections with pancreatin in order to show the reticulated framework of various organs. In this way he succeeded in digesting all of the cells and connective tissue corpuscles, leaving the white fibres and reticulum untouched. After the digestion and shaking to remove the cellular debris, these preparations were mounted and stained. Spalteholz<sup>3</sup> succeeded somewhat later, by means of trypsin, in digesting small pieces of tissue in bulk which had previously been fixed and hardened in graded alcohols or bichloride. Tissue thus prepared, sectioned in paraffin and stained with iron hæmatoxylin, gives very sharp and definite pictures of the connective-

tissue framework. This procedure was very much simplified later by Hoehl,<sup>4</sup> who found that he could, after thorough fixation on the slide, digest thin sections which could then be stained and mounted. Still further improvements of Hoehl's procedure were made by Clark,<sup>5</sup> who stained and digested alternate sections, so that he was able to interpret more accurately by ordinary stained preparations the arrangement of the connective-tissue framework in digested sections.

Somewhat later<sup>6</sup> it was shown that the pictures obtained from the digested frozen sections and the method of piece or slide digestion were practically the same, all of the differences, apparently, depending on differences in the methods of preparation. The disadvantages of the Spalteholz method lay in the fact that, while the connective-tissue fibrils were firmly fixed in situ by the preliminary hardening, the sections were so thin that it was impossible to follow them for any distance. An adequate conception, therefore, of the course of the fibrils in three dimensions could scarcely be formed. By the use of Mall's method this difficulty was partially obviated, and yet the agitation of the sections necessary to free them from the cellular debris often dislocates the fibrils, so that one could not be absolutely certain of their course. Some method, therefore, was needed which would combine the good features of both of the others, one that would not only fix the fibrils absolutely in the position occupied during life, but would at the same time, show their course for a considerable distance in three dimensions. While working in Spalteholz's laboratory and using his method of piece digestion, the writer succeeded, by the use of the stereoscopic microscope and cleared pieces of tissue that had been previously digested in bulk, in demonstrating beautifully the framework of certain organs in three dimensions. The procedure, which is, of course, an extension of Spalteholz's method of piece digestion, may be briefly described as follows:

For the purpose of digestion, the pieces of tissue may be quite large, although in order to permit the free action of the proteolytic enzyme and to facilitate the extraction of the fats, it is scarcely wise to have them exceed 3 mm. in thickness. While it is possible to extract and digest pieces of tissue somewhat thicker than this, no real advantage is gained, inasmuch as the penetration of the stereoscopic microscope does not exceed this depth. It is best, perhaps, to harden fairly large blocks of tissue, and after the hardening to cut them into thinner slabs with a sharp razor, so as to have two nearly parallel plane surfaces on which to use the microscope. Excepting the thickness, the other dimensions are immaterial and can be as great as the nature of the tissue or the work demands. Of the various fixing fluids adapted to this procedure, the mixture of Van Gehuchten

<sup>1</sup> Ewald and Kühne: *Verhandl. d. naturh. med. Ver. zu Heidelb.* Bd. 1.

<sup>2</sup> Mall: *Abhandl. d. k. S. Ges. d. Wiss.*, 1900 and *The Johns Hopkins Hospital Reports*, vol. I.

<sup>3</sup> Spalteholz: *Arch. f. Anat. u. Phys. Anat. Abth.*, Suppl. Bd. 1897.

<sup>4</sup> Hoehl: *Arch. f. Anat. u. Phys. Anat. Abth.*, 1897.

<sup>5</sup> Clark: *Arch. f. Anat. u. Phys. Anat. Abth.*, 1898.

<sup>6</sup> Flint: *Anatomischer Anzeiger*. Bd. XVI, 1899; *Contributions to the Science of Medicine*, dedicated to Dr. William H. Welch by his pupils. Baltimore, 1900. *The Johns Hopkins Hospital Reports*, vol. IX, 1900.

is perhaps the best. It works rapidly, gives good cytological pictures and the chloroform it contains loosens up the fat and thus facilitates the subsequent ethereal extraction. The fluid is made as follows:

Glacial acetic acid.....	10 parts.
Chloroform.....	30 "
Absolute alcohol.....	60 "

Very good results can be obtained with the corrosive acetic mixture, by the use of the graded alcohols, but tissue must not be fixed in formalin, in fluids containing chromic acid or its salts, or those in which osmic acid is an ingredient. Trypsin is powerless to digest tissue that has been hardened in fluids containing any of these reagents. After the fixation it is best to dehydrate the tissue gradually in order to avoid any possible shrinkage. Moreover, great changes in the strength of the alcohols seem to render the digestion of tissue more difficult. After the dehydration is complete the tissue is transferred to ether, placed in one of the filter paper cups and then dropped into the receptacle of a Soxhlet apparatus and is extracted for 5 or 6 days continuously. In Leipzig, the experience with the Soxhlet apparatus had not been altogether satisfactory, and several explosions led them to substitute chloroform for ether in order to escape this danger. The chloroform, of course, does not burn, but at the same time does not seem to extract the fats as well as ether. To overcome this difficulty the Soxhlet apparatus can be placed in a hood and operated by means of hot water obtained from a Fletcher heater situated in another part of the room, or the heater may be placed in the hood and the ether apparatus erected in a sink. In this way all danger of explosions can be obviated and the apparatus may be operated day and night with perfect safety. Prof. Spalteholz writes that he now uses an electric resistance plate to heat the ether flask, a method which is at once safe and economical if the electric current can be obtained. Another method which involves the use of electricity has been devised by Prof. O'Neill, of the Univ. of Cal., which is much simpler than the resistance method used in Leipzig. The ether flask is placed in a snugly fitting cylindrical roll of asbestos board. An ordinary electric light bulb, which generates sufficient heat to keep the ether boiling is then inserted in the cylinder beneath the ether flask. Most laboratories are, however, not wired so that the use of the Fletcher heater in the manner described above offers the only escape from this embarrassing difficulty.

After the extraction has been progressing about a week and all of the free fat is dissolved, the tissue is removed from the apparatus and run down slowly through the graded alcohols. Owing to the well-known fact that CO<sub>2</sub> is less soluble in a mixture of alcohol and water than it is in either of the two fluids alone, there is always an evolution of gas when they are brought together. It is well, therefore, to make up the graded alcohols sometime before the tissue is placed in them, as the gas bubbles become entangled in the meshwork of the connective tissue and often

cause considerable annoyance. After passing through the alcohols the tissues are washed in running water for 24 hours, when they are ready for the digestive mixture. The pancreatin of Parke, Davis & Co. can be used, but for this purpose the preparation manufactured by Grüber after Spalteholz is better adapted to this use. From comparative tests with weighed amounts of pancreatin and fibrin, it appears that Grüber's pancreatin is more potent and more soluble. The resulting solution, moreover, is almost colorless, which is an important consideration in this technique, as the latter quality of the German pancreatin renders the preparations more transparent while the former naturally makes the digestion quicker and more effective. Only a small quantity of the pancreatin need be used. In general enough to cover the end of an ordinary scalpel handle dissolved in 100 cc. of a 0.5 per cent solution of sodium bicarbonate makes a very effective mixture. Inasmuch as the products of digestion inhibit the action of the enzyme, it is better to use a dilute solution of trypsin and renew it often than to make a stronger mixture and allow it to act over a longer period of time. If the fluid is changed every 48 hours, good results, so far as the digestion is concerned, are assured. To prevent putrefaction it is well to use enough chloroform to cover the bottom of the vessel in which the digestion is made. Thymol accomplishes the same result, but has the disadvantage of staining the tissue a dirty brown, which interferes considerably with the sharpness of the picture obtained under the microscope after the digestion and clearing are complete. During the progress of the digestion, the heat of the thermostat volatilizes the chloroform and the digestion mixture becomes filled with small bubbles of gaseous chloroform, some of which often lodge in the meshwork of the connective tissue and cause the digesting organs to float about in the fluid. To avoid this, a small elevated stand can be made out of thick paper which not only keeps the tissue raised from bottom of the beaker when the debris of digestion collects, but keeps the volatilized chloroform away from the tissue. A porcelain filter plate elevated on bits of glass tubing serves this purpose quite as well as the paper stand.

The fats which are united to protein, of course, can only be extracted after the tissue has been submitted to the action of the digestive fluid so that it is necessary to extract and digest at least twice. Apparently the action of the enzyme is much more effective on some organs than others, for in some cases the digestion may be complete after a double extraction and double digestion, while in others it may be necessary to repeat each process four times before the connective tissue is completely free from cellular matter. Among the organs that digest the quickest are the thyroid, spleen, lymph gland and lung, while the salivary glands and pancreas and adrenal digest with much greater difficulty. The pancreas itself is apparently more resistant to its own ferment than any other organ which we have tried. This, of course, applies to the organ only after it has been fixed and hardened, as no experiments were made on the fresh

pancreas. In slide digestions, however, the enzyme apparently acts with great ease, since, owing to the thin sections, all parts are freely exposed to the action of the digestive ferment. In pieces, however, this distinct resistance to the enzyme is noted, and even after repeated extractions and digestions some débris remains embedded in the connective tissue framework. In considering the effect of the nature of the tissue on the digestion we should note perhaps that the method works equally well on pathological as well as normal tissue. The writer has, for example, digested a tumor of the

exactly the form in which it was originally cut. The capsule and the larger and finer processes of connective tissue stand out distinctly. All of the form relations of the organ are distinctly shown in three dimensions. The units of structure, the course of vessels and ducts, the relations of lobules or follicles are preserved and yet rendered transparent so that they can be followed with ease. Even the basement membranes can be made out as a fine web between the limits of the lobules of glands like the submaxillary, parotid, sublingual or pancreas. It is sometimes necessary, how-



FIG. 1.

thyroid which shows perfectly the changes in the framework resulting from the pathological condition in the gland.

One can usually tell from the appearance of the tissue under the microscope when the digestion is complete. As long as any cellular débris can be seen in the meshwork the extractions and digestions must be continued. When, however, nothing but the framework remains, it is thoroughly washed in distilled water and cleared with glycerine. The framework can then be studied with the stereoscopic microscope. A piece of a digested organ forms in this medium a whitish, refractive, translucent block, which preserves

ever, to vary the light in order to bring out some of the finer details. But as a regular routine, all preparations should be studied by means of transmitted and reflected light, with both white and black backgrounds. In this way additional details or different aspects of the same structure are brought into view. As an example of the results obtained by this method, the accompanying drawing of a digested preparation of the thyroid is given. One can note the arrangement and shape of the follicles, the course of the larger blood-vessels and their relations to the units of structure. Outlining the follicles the basement membranes

can be faintly seen. Detailed observations on the thyroid, salivary glands and pancreas, prepared by this method, will appear in a later paper.

After a study of the framework in three dimensions has been made and careful drawings obtained, it is possible, either on the same or another piece of the organ similarly prepared, to investigate the reticulated tissue up to the highest powers of the microscope according to the original method of Spalteholz. The glycerine is washed out and the tissue embedded in paraffin and cut in sections from 4  $\mu$  upwards. Some sections can be stained with iron hæmatoxylin, fuchsin, nigrosin, Mallory's method or in aniline blue alone. Prepared in this way the immersion lens, as was first shown by Spalteholz, gives the finest details of the arrangement of the individual fibres and the smaller fibre bundles. In some way, sections in celloidin give even better results than the thicker sections in paraffin. They can be cut from 15 to 80  $\mu$  thick and stained with an 8 per cent solution of acid fuchsin. Prolonged washing in alcohol removes the fuchsin from the celloidin while the fibrils remain deeply stained. These preparations preserve a suggestion of the third dimension and yet the fuchsin stains perfectly, even the single fibrils.

This extension of Spalteholz's original method yields some fruitful results in the study of the framework of organs, because it fills a distinct gap which has hitherto existed in our technique on the connective tissues. It is a tedious method at best, for it is difficult to get good preparations in less than a month; indeed some of the writer's preparations were extracted and digested alternately for nearly three months. For rapid work Mall's frozen-section method will still be of service to us, and the methods of Spalteholz and his pupils will always be required in studying the framework of an organ in order to give us control pictures in ordinary stained preparations.

#### EXPLANATION OF THE FIGURE.

Fig. 1. Framework of the human Gl. thyreoides from a male about 45 years of age.  $\times 13$ .

The preparation does not include a portion of the capsule, but is cut from the middle of the gland. The follicles closely packed together are separated from each other by the basement membranes and a slight amount of inter-follicular connective tissue. The course of the vessels can be followed into the depths and the shape of the superimposed follicles easily made out.

## THE TOXIC EFFECT OF ALCOHOL ON THE GANGLION CELLS OF THE RETINA.<sup>1</sup>

### ABSTRACT.

BY HARRY FRIEDENWALD, M.D., Baltimore.

Ward A. Holden, in 1899, reported that he had given a dog methyl alcohol, had produced amblyopia and on examining the retina by Nissl's method had found sufficient evidence of degeneration in the ganglion cells to lead him to the conclusion that it is this degeneration that produces the amblyopia. Since then Birch Hirschfeld has investigated the effect of methyl alcohol (as well as that of a number of other poisons). He experimented on rabbits and on chickens, and gave sufficiently large doses to produce intoxication. The animals rapidly lost weight and soon died. The retinæ all showed marked signs of degeneration in the ganglion cells, and in one case changes were found in an optic nerve very suggestive of the lesion observed in man in chronic alcohol and tobacco amblyopia. Objection has been raised against accepting these experimental results on animals as necessarily identical with the effect of chronic alcohol poisoning on man, and the differences in the clinical features of acute methyl alcohol and of chronic ethyl alcohol blindness have been

pointed out. In order to obviate these objections the writer used various forms of alcohol in smaller doses over an extended period (almost four months). Pure and commercial methyl alcohol, absolute ethyl alcohol and essence of Jamaica ginger made of 95 per cent ethyl alcohol were employed, and the animal selected was the rabbit. The period of experimentation was sufficiently long, as was shown by the high degree of cirrhosis of the liver found in the rabbit fed with absolute ethyl alcohol. The animals were all in apparently good health when killed.

The effects of all four substances were alike. The retinal ganglion cells showed marked degeneration and the inner and outer nuclear layers were less affected. It was evident that methyl and ethyl alcohol act similarly on the retina in chronic poisoning, and that the degenerative changes produced by chronic alcohol poisoning are similar to those found by Holden and by Birch Hirschfeld in acute methyl alcohol poisoning.

These experiments are the first in which ethyl alcohol has been used, as well as the first in which degenerative changes have been demonstrated in chronic alcohol poisoning.

<sup>1</sup> Paper read at Neurological Section Med. and Chir. Faculty of Maryland, Dec. 13, 1901.

## PROCEEDINGS OF SOCIETIES.

## THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

*October 7, 1901.***Exhibition of Medical Cases, Primitive Spleno-megaly with Anæmia, Cirrhosis of the Liver and Jaundice.—Banti's Disease. DR. OSLER.**

We have been much interested of late in cases of enlarged spleens, occurring independently of leukemia, malaria and the chronic, passive congestion, such as occurs in cirrhosis of the liver and diseases of the heart. Our cases may be divided into four groups: 1. Cases of enlarged spleen in otherwise perfectly healthy persons who have no marked anæmia, and who suffer only with the mechanical discomfort of the greatly enlarged organ. 2. Cases with changes in the blood not unlike those of pernicious anæmia. In one instance the enlarged spleen disappeared under treatment but the woman relapsed a year later and died. Several of our cases of enlarged spleen in young children come in this group. 3. Primitive spleno-megaly of long duration—8, 10 or 12 years—with an anæmia of the chlorotic type, a special tendency to hemorrhages, particularly from the stomach, and in some cases with pigmentation of the skin; and 4. A group of cases with anæmia, enlarged spleen, cirrhotic liver and jaundice. This last group of cases was studied by Banti and the condition is sometimes called by his name. The case before you is, I believe, a good illustration of this variety.

The woman is 40 years of age, and came in complaining of swelling of the abdomen and legs with pain in the back. She had suffered the usual infantile and infectious diseases and had pneumonia 8 years ago. Eleven years ago she had malaria for the first time and then for four successive years had chills in spring. The tumor in the abdomen has been present since the first malarial attack. During the first four years it grew but has not increased in size since. When admitted August 3, 1898, the tumor measured 17 cm. and she had ascites. Blood examination then showed hæmoglobin 47 per cent, red cells 2,500,000, leucocytes 2500. When discharged September 30, the hæmoglobin had risen to 50 per cent, the red cells to 3,500,000 and the leucocytes remained about the same. The patient entered the hospital again September 30, of this year, having been fairly well and able to work during the interval. Jaundice had existed for about a month, and for two weeks before admission she had headache and œdema of the feet and legs. On admission there was a moderate ascites. The edge of the liver could be readily felt and was evidently cirrhotic; the spleen extended 18 cm. from the left costal margin and 15.5 in width. The blood examination was interesting when contrasted with that of 2 years ago. The hæmoglobin was 75 per cent, the red cells 5,760,000 and the white cells 4370. She has a few of the papillary angiomas of the eyelids.

That she has cirrhosis of the liver in addition to the chronic enlargement of the spleen is, I think, most probable.

The cases belonging under group 2, discovered accidentally, are apt to be mistaken for ovarian tumors, in fact, in some of the early cases of removal of the spleen in this country this mistake was made.

## DISCUSSION.

DR. HUNNER.—It may be of interest to state that we have a case of this kind in the wards now, about ready to go home, upon whom the diagnosis of ovarian cyst was made. She was 29 years of age and the tumor was discovered three years ago after the birth of a child. She had no particular discomfort from it but complained of weakness and indigestion in addition to the presence of this enlargement. On bi-manual examination a large tumor was felt choking the true pelvis. The notch was plainly felt and the upper portion was considered to be another lobule of the cyst, particularly as we often find dermoids lying in this position. At the operation it was found to be an enlarged spleen in the pelvis. Fortunately, Dr. Schenk had looked up the two other cases that have been operated upon in our department and knew that neither had suffered any particular trouble following the loss of the spleen, but were living and in good health, and so we removed this spleen and the patient has done perfectly well.

DR. OSLER.—Were all three of these cases mistaken for ovarian tumors?

DR. HUNNER.—The first was diagnosed as an ovarian cyst, and the second was thought to be a cystic kidney.

**Gastrotomy for Removal of False Teeth. DR. FINNEY.**

In 1886 Dr. H. Richardson, of Boston, reported the first case of gastrotomy for the removal of a plate of false teeth from the lower portion of the œsophagus. Shortly after, Dr. Bull, of New York, reported the removal of a peach stone from the lower portion of the œsophagus through a similar incision.

In 1892 I reported in the *JOHNS HOPKINS HOSPITAL BULLETIN* a third case of gastrotomy for the removal of a peach stone from the lower end of the œsophagus, and two years later I operated upon a second case almost identical with the first. These four cases all recovered. Since this time many similar operations have been reported in the literature.

To-night I show a patient upon whom I operated ten days ago for the removal of a plate, containing one false tooth, which had been swallowed during sleep. In this case I performed a preliminary œsophagotomy, thinking it might be possible to remove the plate through the œsophageal wound. This proved impossible, however, because the prongs of the plate, which held it in place, pointed upwards as the plate lay in the œsophagus, and prevented its being withdrawn. I could push it down, but could not withdraw it, as those prongs engaged at once in the mucous membrane. It was lodged about the level of or a little below the cricoid cartilage.

Finding it impossible to withdraw it, I pushed it down as far as I could with a pair of forceps, and then opened the stomach through a median incision. With my hand in the stomach, and a finger through the cardiac orifice, I could just touch the plate, but could not remove it. I then made use of the same procedure used in my preceding cases, namely, passed a bougie from below upwards through the abdominal wound, the wound in the stomach, the cardiac orifice, the œsophagus, and then brought it out of the patient's mouth. To the end of the bougie a strong string was tied, and to this a small sponge was attached. The sponge was then drawn down through the patient's mouth into the œsophagus and thus the œsophagus was thoroughly swept out and the dental plate brought down into the stomach, whence it was readily removed by the fingers. The stomach contained a large amount of undigested food and it was with difficulty that the peritoneal cavity was kept from soiling with stomach contents. The stomach wound, which was about two and one-half inches long, was closed with mattress sutures and the abdomen closed without drainage.

The œsophageal wound was also closed with mattress sutures, and an iodoform gauze drain carried down to the line of sutures and the skin wound left open. There was no leakage from the œsophagus at all and the patient made an uninterrupted recovery. My first peach stone case was complicated by a periesophageal abscess which I subsequently drained through the posterior mediastinum, after resecting a portion of one rib.

#### Excision of the Gall-Bladder. DR. FINNEY.

I wish to report to-night four cases of excision of the gall-bladder in which I have made use of a new method of procedure. It differs from other methods in that one reflects from the fundus of the gall-bladder lateral flaps of the peritoneal and muscular coats of the gall-bladder which cover up the raw area left on the under surface of the liver. The steps in the operation are as follows:

The gall-bladder is exposed in the usual way and the peritoneal cavity thoroughly protected by a gauze packing. Parallel incisions are then made beginning at the fundus and extending upwards toward the neck of the gall-bladder. These incisions should be made on either side far enough from the attachment of the gall-bladder to the liver so that when the gall-bladder has been removed these peritoneal flaps may be replaced and thus cover completely the denuded surface of the liver.

The incision should be carried down only through the peritoneal and muscular covering of the gall-bladder, and then with a small, blunt dissector, or the finger, the gall-bladder can be rapidly separated from its attachments to the liver. Toward the neck of the gall-bladder the reflection of peritoneum forms a mesentery-like attachment to the cystic duct. The two peritoneal layers are so close here that they cannot readily be separated, so one divides the fold just as one would divide the mesentery in an intestinal resection. This dissection is carried up to the junction of the

cystic and common ducts. Here a peritoneal cuff is reflected just as in an appendicectomy; the cystic duct and artery are ligated close to the common duct, the peritoneal cuff is then inverted over the raw end of the cystic duct, which has been treated in the same way as the stump of an appendix. The free edges of the peritoneal flaps which have been reflected on either side from the fundus and body of the gall-bladder, are then brought together by a few sutures and in this way the raw surface of the liver is completely covered in. The gall-bladder is thus removed intact without opening it and without in any way soiling the peritoneal cavity.

I have made use of a stitch or two taken in the fundus of the gall-bladder, which serve very well as retractors or handles to the gall-bladder during the necessary manipulation.

In my last case the operation was accomplished so quickly and satisfactorily, and the hemorrhage was so insignificant, that I felt justified in closing the abdominal cavity without drainage. This patient has made a most satisfactory recovery.

Of course this operation is best carried out in those cases in which the gall-bladder is distended and its walls thickened. In two of my cases the gall-bladder was very adherent to surrounding structures, but this interfered very little with the operation. In the case of a contracted gall-bladder, the steps of the operation would have to be modified somewhat, that is, in taking one's peritoneal flaps.

The chief advantages of this operation over others are that the gall-bladder is removed unopened and the possibility of infection from this source is thus done away with. The raw surfaces are covered over with peritoneum, thus lessening the danger of adhesion. Drainage is unnecessary.

It would seem as if the analogy drawn by certain writers between the appendix and the gall-bladder was well founded; the function of neither organ is entirely understood; both are fruitful in the production of trouble; both can be dispensed with without any inconvenience on the part of the patient.

The anatomical structure of the appendix and of the cystic duct renders them both amenable to the same treatment, that is, ligation excision and investment of the stump with peritoneal covering. In a subsequent paper upon this subject, we propose discussing at greater length the indications for and advantages of cholecystectomy over other operations upon the gall-bladder.

My four cases have all made rapid and complete recoveries. In the first three I made use of an abdominal drain of iodoform gauze carried down to the stump of the cystic duct; no leakage occurred in any of these cases. In my last case I closed without drainage. In all four cases the gall-bladders were large and distended, containing from one to several hundred gall-stones.

#### DISCUSSION.

DR. HALSTED.—To close the stump of a cystic duct after cystectomy in such a way that it will not leak during the process of healing is a matter which will surely interest all

surgeons experienced in the surgery of the bile passages. A biliary fistula worries and often weakens a patient, and reminds the surgeon most unpleasantly that the surgery of the bile passages is not a closed chapter. I cannot quite agree with Kehr, who well deserves to be recorded as an authority in this branch of surgery, that a biliary fistula after ectomy is of so little consequence. Nor do I believe that the drainage of the stump of the cysticus with the expectation of a fistula is an ideal surgical procedure. Furthermore, from our comparatively small experience, I should not suppose that it would be necessary to drain a ductus hepaticus in about 37 per cent of all operations for gall stones.<sup>1</sup>

So the temptation to close the cystic duct in certain cases is irresistible. Last spring, with this object in view, I made a cuff from the outer coats of the cystic duct, but the cuff was too short to satisfactorily effect a solid closure of the ligated and sutured duct. It was my intention to make this cuff long enough at the next cystectomy. In the meantime Dr. Finney has carried this plan to its limit and has enucleated the gall-bladder, as well as the cystic duct. So successful was he that in one of the two cases, which he has to-night reported, he confidently closed the abdomen without drainage. Kehr would as confidently predict a second operation for a certain portion of cases so treated, and last year he still urgently recommended drainage, not only of the wound, but also of the bile passages. Mayo Robson, in his book "Diseases of the Gall-Bladder and Bile Ducts," describes a procedure which probably embraces mine and Dr. Finney's also. He speaks of stripping the *peritoneum* from the top and back of the gall-bladder and from the entire circumference of the cystic duct, and utilizing this coat to cover the stump of the cystic duct in cases of excision of the gall-bladder. As he could hardly make a flap of peritoneum only, it is likely that he would do what Dr. Finney did in the two cases reported to-night. It is possible that William J. Mayo, in excising the mucous membrane of the gall-bladder, would take about the same route between the coats. The thickness of the peritoneo-fibro-muscular flap would vary considerably.<sup>2</sup>

Some sure and simpler method must be devised for determining positively the presence of stones in the ductus choleduchus after excision of the gall-bladder.

#### Exhibition of Surgical Cases. DR. FOLLIS.

CASE 1.—This patient, aged 11, was shot in the abdomen with a 22-calibre revolver 2½ hours before admission. He had taken a full meal five hours before the accident. On

admission his temperature was 99.4°; pulse 114; leucocytes 35,000. The wound of entrance was at the left of the umbilicus and about at the middle of the left rectus muscle. He was operated upon three hours and fifty minutes after the injury, the incision being made in the course of the bullet. Considerable bloody fluid was found in the peritoneum. There were three small perforations in the jejunum and the bullet had gone through the mesocolon and lodged somewhere posteriorly. The three perforations were sutured, the general peritoneal cavity was wiped out, and a piece of iodoform gauze was left at the point from which some hæmorrhage seemed to arise. The bullet was not found. He was very much shocked, and after the operation the pulse reached 160. For the first five or six days he was in a precarious condition. He was given infusions, stimulating enemata, and strychnia. Nothing was given by mouth until after the bowels had moved spontaneously, on the fifth day. Only liquids were given until the tenth day, when soft diet was allowed. He made a very good recovery. Only three perforations were found at operation, but there was probably a fourth, which took care of itself. An X-ray photograph taken after the operation showed the bullet embedded in the psoas region.

CASE 2.—This patient, a German, aged 71 years, was admitted on September 1, with a strangulated right-sided inguinal hernia, which had never previously been strangulated. Strangulation had occurred twelve hours before entrance.

The general condition of the patient was good; pulse 70; temperature 100°; leucocytes 14,000. While preparations were being made for operating, his feet were elevated and an ice bag applied over the tumor. Two doses of morphia were given, as a preliminary step to cocaine anæsthesia. Under local anæsthesia, cocaine 1-1000, an incision was made in the right inguinal region. The aponeurosis of the external oblique was divided, and the ileo-inguinal nerve was found, cocainized, and divided. A large mass of indurated omentum was found in the sac, together with a loop of gangrenous small intestine 24 cm. in length. The constriction was relieved, and the loop of strangulated bowel with seven or eight cm. of good intestine on each side was brought out and left on the abdominal wall. Gauze was packed loosely about this. This was done to see whether the bowel would clear up, as had happened in two cases of Dr. Mitchell's, in which the bowel seemed in bad condition at the time of operation, but which after twenty-four hours he was able to replace. After twenty-four hours the bowel appeared green, and a resection was done and an end-to-end anastomosis made, using Dr. Halsted's rubber bag. This procedure was carried out entirely outside the general peritoneal cavity, which was walled off by gauze and 24-hour adhesions. The field of operation was then cleaned and the bowel was replaced in the cavity, and a small gauze drain inserted to point of suture. This second operation was done entirely without anæsthesia, with the exception of two ½ gr. doses of morphia, one given an hour before, and one at the beginning of the

<sup>1</sup> "Of 84 laparotomies for gall-stones there were 28 simple ectomies and 31 combined with drainage of the hepatic duct."  
—Kehr, Verhau. d. Deutsch. Ges. F. Chirurg., 1900, pp. 172.

<sup>2</sup> In a case recently operated upon by me, it was so difficult to enucleate the gall-bladder that I twice entered it, before and behind on the same parallel, but could easily strip a flap from the cystic duct; with this I effected a satisfactory closure, but I thought it safer to drain down to the stump.

operation. The excision and suture were entirely painless; but when the parietal peritoneum was manipulated in replacing the bowel, the patient complained of pain. An uneventful recovery followed.

Since the opening of the hospital, eleven cases of strangulated hernia with gangrene of the bowel have been admitted. In four of these an immediate end-to-end suture was done. One of these patients recovered. Four other cases were treated by excision of the gangrenous portion of the bowel and the formation of an artificial anus, with the idea of doing a secondary suture later. Two of these died before the second operation; the other two died after the anastomosis had been made. In one case, the strangulated loop was thought to be viable and was returned to the peritoneal cavity, but evidently it was not and the patient died of peritonitis. One case of Dr. Bloodgood's was treated like the present one, except that the bowel was sutured to the parietal peritoneum and the general cavity was opened at the second operation before the suture was done. This patient had a general anæsthetic at the second operation, and died of broncho-pneumonia.

#### DISCUSSION.

DR. FINNEY.—I would like to report in this connection an interesting case which is as yet unreported. I was called about three years ago to see an old lady with a femoral hernia which had been strangulated for four days. Her condition was very weak and precarious at the time. I cut down upon the hernia and found a loop of intestine, strangulated, black, and beginning to be gangrenous. Her condition was such that I simply pulled the intestine out into the wound after having relieved the constriction, packed it about by gauze and left it. During the following night she was very restless and vomited violently, due, apparently, to the ether.

During her straining she forced out two or three feet of small intestine into the dressing. This was replaced the next day by Dr. Bloodgood, in my absence, and he then made an opening into the gangrenous loop; this was followed by immediate relief of her distention. I had not opened the loop at the time for fear of soiling the peritoneal cavity, intending to wait until protective adhesions had been formed.

The patient from this time made an uninterrupted recovery, except after we began to feed her by the mouth, it was noticed that in a short while quantities of partly digested food poured out of the abdominal fistula and she began to lose weight rapidly.

Dr. Pancoast, the resident surgeon of the Union Protestant Infirmary, of which institution the patient was an inmate, overcame this loss of intestinal contents by a very ingenious procedure. He inserted a rectal tube into the lower opening of the bowel and with a funnel inserted into the upper end of the rectal tube, he, by placing the patient upon her side, caught the intestinal contents as it poured out of the upper opening in the bowel. In this way he bridged over the break in the continuity of the intestinal canal with very little loss of intestinal contents.

The patient at once began to pick up in weight and strength, and after two or three weeks, became quite strong and robust again. I then cut down upon the fistula, and found that the strangulated loop of bowel had occurred in the very uppermost portion of the jejunum, which explained the patient's sudden loss of weight.

I did an end-to-end anastomosis with the aid of Dr. Halsted's rubber bags, and the patient made an uninterrupted recovery, and is now alive and well some three years after the operation.

#### A Case of Labor in a Bicornate Uterus. DR. BETTMANN.

Mrs. R. W., aged 35, without any history of apparent deformities in any member of her family, had given birth to eight children at term and had miscarried once. Three of her labors had been by the occiput and four by the breech, the last two children being born dead.

*Present pregnancy.*—Normal except for some hemorrhage throughout the last week. Pelvis normal.

*Labor.*—Seen for the first time by the Out-Patient Department twelve hours after onset. L. S. T. T. Frank breech. What was thought to be a marked cystocele protruded from the anterior wall of the vagina. Cervix was half dilated, soft and non-resistant. The breech was just entering the superior strait. The heart during the time we were in attendance (four hours, circa) had been well heard to the left of the umbilicus, when suddenly it was discovered to be inaudible. Internal examination showed that the breech had rotated into a posterior position, so that the sacrum lay directly parallel to the sacrum of the mother. The cord of the child was palpated and was found to be pulseless. Extraction was undertaken in the interests of the child, which was delivered within ten minutes but could not be resuscitated. In the manipulation, consisting of alternate traction in each, given by means of the index finger, a partial vaginal septum about 3 cm. in breadth was discovered in the middle third of the vagina, running from the anterior to the posterior wall directly in the mid-line. The probable diagnosis of double anomaly of the uterus was made, thus accounting for the persistence of breech presentation and the abnormal rotation of this breech. The child was a male weighing seven pounds, and showed at autopsy only the signs of intrauterine asphyxia. The patient died 36 hours after labor. She had apparently been doing perfectly well up to within an hour before death, the only anomaly in the puerperium being retention of urine and a small external hemorrhage eighteen hours before death.

The autopsy revealed a uterus bicornis unicollis, with rupture through the lower uterine segment of the left (pregnant) cornu, extending a slight distance into the vagina. The rupture did not extend above the contraction ring (which was well marked), so that the extravasation of blood resulting therefrom was subperitoneal and not intraperitoneal. All of the pelvic connective tissue of the left side was infiltrated with clotted blood, which also extended across the

median line and up the rectum as high as the sigmoid flexure. All the other organs were normal.

Dr. Bettmann then discussed the various types of double anomalies of the uterus, illustrating these by means of diagrammatic charts. He spoke of the embryological and obstetrical significance of the various types and explained the rupture of the uterus in his case in the following manner:

The axis of the pregnant cornu deviated 45° from the axis of the pelvis, so that traction made in the axis of the pelvis exerted force directly against the lower uterine segment instead of along the axis of the uterus. The position of the tear upholds this theory, for it is in the left side of the lower uterine segment (the left cornu being the pregnant one). At the time extraction was undertaken the presenting breech had not yet cleared the cervical rim, so that traction upon it pulled it directly against the lower uterine segment.

*October 21, 1901.*

Dr. William Osler was elected President of the Society for the ensuing year and Dr. Hunner was re-elected Secretary.

#### **Exhibition of Medical Cases, Post-Typhoid Insanity. DR. McCRAE.**

This case is of considerable interest on account of the rarity of the condition, namely, marked mental symptoms following typhoid fever. Since some of you saw him in the clinic last week he is convalescing from the fever but he is still showing marked mental features. Briefly the history is that the patient was admitted on the 14th of September with fairly severe symptoms of typhoid. He ran an ordinary course as far as the fever goes and is now at the end of the sixth week. Early in the disease he showed marked mental symptoms, being delirious and later suffering from delusions. This was followed by a period of melancholia, but within the last 48 hours he has again shown a change, and this time for the better, so that it looks now as if he would soon be well.

Various classifications have been made of the insanities following typhoid fever. I should find difficulty in putting this case under any of those definite headings. The prognosis is exceedingly good, for there is every chance that his mental condition will clear up entirely.

#### **Adherent Pericardium.**

This case is shown not so much on account of the special features of the case but rather as the type of a condition of interest to us clinically. The reproach has often been made that the pathologist makes many of our diagnoses for us, and possibly first on the list of such conditions is that of adherent pericardium.

This boy has a rather puzzling heart. He is 19 years of age and came in complaining of shortness of breath. In April of this year he was in a hospital at Harrisburg with what he thinks was rheumatism, but states that he had

attacks of shortness of breath prior to that time. He has been here now since September 27 and has made very little progress. On inspection we find some precordial bulging which suggests that the illness has been of longer duration than the history would lead one to suspect. The heart is slightly enlarged and there are some indefinite and variable murmurs. He has none of the classical symptoms of adherent pericardium, but a striking thing to my mind is that he has not improved under treatment and that he has a slight systolic retraction, about the third or fourth interspace, with no retraction behind and no fixation of dullness.

In this connection I want to show a specimen from a patient that has been in the ward within the last few days, and in this case we had been able to follow the history from the onset, so far as the heart symptoms were concerned. The man was 56 years of age and admitted in January of this year for a sudden attack of acute pericarditis, which was regarded as idiopathic, and at the end of two weeks he was discharged apparently well. He was readmitted in April with a history that was significant. Two days previously he had an attack of shortness of breath with sudden pain and dyspnoea. The heart was slightly enlarged. Within a few weeks he was again discharged, apparently well, but in June he returned for another brief stay and in September he returned and remained until his death. We thought the man had adherent pericardium from the attack of pericarditis, the acute onset of the myocarditis and the subsequent history. The specimen here shows a generally adherent pericardium.

Now briefly to speak of one or two points in pericarditis. First, we must bear in mind that pericarditis means often an involvement of the myocardium and even of the endocardium. A man who runs the whole course of his myocarditis in 6 months may be spoken of, I think, as an acute case. In this specimen there was a well-marked myocarditis as well as a pericarditis. Such a case as the patient had shown will rarely be diagnosed from the physical signs. Any one looking at this boy for the first time, say a week ago, would probably not make the diagnosis. It impresses me, however, much the same way as the other case I have referred to which we were able to follow throughout the whole course. The symptoms are out of proportion to any discoverable lesion, and he shows no signs of improvement.

#### **DISCUSSION.**

**DR. HURD.**—It is evident that in the case shown of post-typhoid delirium the patient has suffered from a prolonged exhausting disease and the condition of apparent depression following such exhaustion is not unusual. The mental faculties were evidently temporarily exhausted from the delirium but the state of the patient is not one of acute distress, such as is characteristic of true melancholia. In some cases the mental aberration of a typhoid fever patient is not recognized. In two instances that have come to my knowledge, patients who had given no evidences of mental aberration during the attack of typhoid fever made and signed their

wills. Two or three months after when fully convalescent both were much astonished to learn that wills had been executed. Unquestionably the mental state of these persons must have been an unnatural one at the time the wills were made, yet it did not attract the attention of friends and bystanders or the lawyers who drew the wills.

#### **Exhibition of Pathological Specimens. DR. MACCALLUM.**

The patient, a boy, entered the hospital in September, having passed through an indefinite illness in the Charity Hospital in New Orleans during the preceding winter. He was deeply jaundiced, passed very little urine, and that deeply bilestained and containing besides albumen and casts, leucin and tyrosin. After several days of delirium he died.

At the autopsy there was marked ascites and the abdominal organs were very much congested. The liver, however, showed the most extensive changes. It was very small, tough and flabby. From the dorsal surface of the right lobe there projected a large dark green nodular mass, and similar but smaller masses could be seen on the under surface. On a section through the whole liver these stood out sharply from the remaining substance; they had a general lobular arrangement, differing from that of a normal liver in the great size and irregularity of the lobules. The remaining liver substance was grey brown in color, showed very indefinite lobulation and resembled that seen in the condition of senile atrophy.

Microscopically the nodules appeared to be the most nearly normal of the tissues found in the liver. They appeared like greatly enlarged liver lobules in which the radiate order of the liver cells is much disarranged, and often the relations of central and peripheral blood-vessels were not to be made out. The cells in these masses were often very atypical in appearance. The remaining liver substance showed roughly the ordinary lobulated appearance, but the liver cells were practically lacking, the radiate appearance of the lobule being maintained by the arrangement of the capillaries and the greatly thickened intervening connective tissue. In the periphery great numbers of newly-formed gall-ducts were visible branching from the interlobular gall-ducts to push into the lobule toward its centre. These often anastomosed toward the centre and the cells there had taken on to a certain extent the appearance of liver cells.

As it is known that in acute yellow atrophy the destruction of cells is marked on the periphery of the lobule, it seems probable that these must be considered as entirely new formed from the interlobular gall-ducts. The case corresponds almost exactly with those described by Marchand and Stroebe, who explain the condition as the result of acute yellow atrophy, recovery from which is associated with attempts at regeneration on the part of the liver, this regeneration being carried out either by the formation of large nodules from portions of the liver which have escaped destruction or by a diffuse proliferation of the bile-ducts, whose cells may reform liver cells and take on their functions.

#### **The Importance of the Adducted Position in the Normal and Weakened Foot. DR. SAMPSON.**

(See January BULLETIN, 1902, page 8.)

#### **DISCUSSION.**

DR. HURD.—Those who have not followed Dr. Sampson's work will be interested to know that by means of shoes made upon the lasts devised by him a number of physicians of the Hospital who suffered from flat foot, because of constant standing in the operating rooms, have found themselves greatly relieved.

#### **Pathological Report of a Fatal Case of Enteritis with Anæmia Caused by Uncinaria Duodenalis. DR. YATES.**

(See December BULLETIN, 1901, page 366.)

November 4, 1901.

The meeting was called to order by Dr. Hurd.

#### **Indurated Scrofulous Erythema, Exhibition of Case. DR. GILCHRIST.**

This patient presents an eruption on the skin which forms one of a very interesting group of diseases. It is a rare form of skin disease and I think is the only case we have seen in the dispensary. The patient is a young girl of 19 years who applied for treatment, on the first occasion, about 20 months ago, when she showed on the left leg a chronic lesion which on a cursory examination looked like a syphilitic patch. The lesion measured 5 by 6 cm. and was of a dull reddish color, very much indurated, and presented two or three punched out ulcers with undermined edges. There was a family history of tuberculosis but none in the patient though she was anæmic and much run down. A guinea-pig was inoculated with scrapings from the largest ulcer and the animal died within 24 hours, but not of tuberculosis. The patient got well under treatment by the use of iodoform applied locally and Blaud's pills given internally. She now reappears with similar new lesions on the right leg, one patch being almost an exact reproduction of the first lesion. A portion of this ulcer has been curetted and guinea-pigs inoculated subcutaneously; the animals are still living. One small ulcer was excised and the sections from the tissue did not show any tuberculous structure, nor were any bacilli found.

There is a group of diseases of the skin, such as lupus vulgaris and tuberculosis cutis, which can be definitely determined to be tuberculosis of the skin. There is also the warty form of tuberculosis which occurs on the knuckles usually from inoculation. Then there is a second group of diseases mentioned under a variety of names with the history of tuberculosis in the family but where only recently have tubercle bacilli been discovered in the local lesions. One of this group is *Erythema Induratum Scrofulaceum*, of which this case is a typical example. Quite recently McLeod, of London,

has demonstrated the presence of tubercle bacilli in the tissues, which fact places this disease in the first group. This group also contains the scrofulous gumma with broken down glands, lichen scrofulosorum, acne varioliformis, scrofuloderma and the necrotic granuloma, a form which has been described under many names, but it seems to me the nomenclature might be very much simplified if they were all grouped under the one heading of tuberculosis of the skin and given different names according to the clinical pictures, just as we do in the case of ring-worm where the parasite is practically the same but the name differs according to the location of the lesion.

**A Case of Estivo-Autumnal Fever with Unusually Few Parasites in the Peripheral Circulation.** DR. THAYER.

The patient that I wish to show you this evening is a young woman, 18 years of age, who was admitted to the hospital on the 8th of September. There are no facts of importance in her family or personal history excepting that in the spring and fall of 1900 she suffered from chills and fever. Five days before entrance she began to complain of general malaise and on the following day had a chill. This was repeated on the succeeding day, and two days later she took to bed. On entrance the physical examination showed little of importance; the temperature was 100.7°; the thorax and abdomen showed nothing remarkable; the spleen was not palpable; there was some hypogastric tenderness, due probably to a distended bladder. The colorless corpuscles were reduced in number. No malarial parasites were found after several examinations.

The temperature fell gradually, reaching a normal point on the 12th of September, four days after entrance to the hospital, and remained normal during five days. On the 17th it touched 99°. On the 19th it rose again to a point a little above 99°, and on the evening of the 21st it was a little above 100°. On the 22nd there was a chill followed by fever. The temperature remained elevated somewhat over twelve hours, just how long it is impossible to say as it was not recorded with sufficient frequency. At 8 A. M. on the 22nd it was normal, but in the evening it rose again to 101.3°, reaching the normal point on the morning of the 23rd. Again on the 23rd there was a febrile paroxysm, the temperature reaching 103° and falling gradually to a subnormal point on the evening of the following day. During this time the patient complained much of headache and of abdominal pains localized for the most part in the region of the bladder. There was retention of urine, necessitating catheterization. Repeated examinations of the blood failed to show malarial parasites. Several counts of the leucocytes were made, showing always a subnormal number. Over the right clavicle there was slight dulness; the expiration was somewhat prolonged, and on several occasions a few fine moist râles were heard. Later there was tenderness in the region of the spleen. From the 26th to the 30th there was slight, rather irregular fever ranging between 98.5° and 101.5°. On the 2nd of October the temperature rose to 103.2°, and on the

following day it again touched a point about 103°, varying during the next week between normal and 103°. The fever continued, the temperature occasionally remitting but never falling below 98.5° until the 14th of October.

During this period the blood had been repeatedly examined without result, but on the 14th a moderate number of crescentic and ovoid æstivo-autumnal parasites were found. Hyaline bodies were found on the following day. Treatment by quinine was started immediately—0.325 (gr. V) every four hours. The temperature fell to the normal point on the following day and has remained normal or subnormal ever since. The spleen, which at first was impalpable, was just to be felt in the latter part of her illness and was distinctly tender on palpation.

No hyaline forms were noted after the 15th of October, though two ovoid pigmented bodies—gametocytes—were found on careful search on the 4th of November, two days before discharge.

There are several points in connection with this case to which I should like to direct your attention. (1) The irregular and continuous fever. Such charts, due solely to malarial infection, are not common in these regions; yet they are occasionally met with and the explanation is not difficult.

The remarkable periodicity of the febrile manifestations, one of the most striking symptoms of malaria is, as is well known, especially marked in tertian and quartan infections, where the paroxysms occur with almost clock-like regularity.

The cause of this periodicity is intimately associated with the life history of the parasites. The tertian and quartan organisms exist in the blood in great groups, all the members of which pass through their life cycle in unison, the sporulation of all the parasites in such a group occurring within relatively few hours, and the paroxysms have been shown to be definitely connected with the sporulation of these groups of parasites. Every now and then, however, one finds, even in tertian and quartan infections, the presence of a multiplicity of groups, or a tendency toward lack of the definite arrangement of the parasites in groups which, as one might expect, results in the occurrence of more or less irregular or continuous fever. This, however, is very unusual in tertian and quartan infections.

But in æstivo-autumnal fever the state of affairs is different. The majority of cases of æstivo-autumnal fever in this climate show well defined and fairly regularly intermittent fever with chills. In many cases, however, the fever if untreated tends to become continuous or irregular. This is probably due chiefly to the development of a multiplicity of groups of parasites or to the spreading out of the period of sporulation of the existing groups, so as to unduly prolong the paroxysms until they overlap one another. In æstivo-autumnal fever, as has been repeatedly observed, the characteristic stages of the paroxysm are often absent—"dumb chills."

It has also repeatedly been shown that insufficient treatment with quinine tends to disturb materially the regularity

of the fever. It is not impossible that this depends upon an interference with the development of some of those parasites which are not actually destroyed, which results in a disturbance of the regular arrangement in groups.

(2) The second point to which I would call your attention is the remarkable scarcity of parasites in the peripheral circulation. There was considerable question as to the nature of this case. The suspicious signs at the right apex, as well as the nature of the chart, suggested that the fever might be due to an incipient tuberculosis. Typhoid fever was thought of but was not considered probable.

Could such a fever be due entirely to malaria without the discovery of the parasites in the blood on reasonably careful examinations? How are we to account for the gradual disappearance of fever after entrance?

A very interesting fact has been developed on close questioning of the patient, namely, that after the first chill she took two doses of quinine of uncertain amount. This, together with the favorable conditions, rest in bed, and general treatment in a hospital, doubtless accounted for the temporary disappearance of fever, and also, in part, for the absence of parasites on entrance to the hospital. The reduction in the number of leucocytes, the clearing up of the suspicious signs at the apex, and the absence at all times of expectoration, rendered the diagnosis of tuberculosis improbable. There was little, on careful observation of the case, to suggest typhoid fever, and the absence of Widal reaction even at this late period speaks against it. These facts, in connection with the specific effect of quinine, leave little doubt that the case was, from beginning to end, due to malarial infection. The great infrequency of the parasites in the peripheral circulation is an extremely rare occurrence, but it is well to recognize the fact that it is a condition occasionally met with. In quartan fever the parasites are found at all stages of their development in the peripheral blood as well as in the spleen and internal organs. In tertian infections the state of things is a little different, in that the parasites are found during the latter stages of development with much greater frequency in the blood of the spleen than in the peripheral circulation. In the majority of instances of æstivo-autumnal fever this tendency is more marked, in that only young forms are found in the peripheral circulation, and often in cases where the parasites are fairly well arranged in groups, few, if any, organisms are to be found in the peripheral circulation during the paroxysm. But there are cases, like that before us, in which almost the entire cycle of development of the parasites takes place in the internal organs, where examination of the peripheral blood, at whatever period it may be made, reveals but very little. The same condition may be seen—with great rarity, however—in tertian infections. Happily, those instances of æstivo-autumnal fever in which the parasites are not to be found in the peripheral circulation, are rarely cases of great severity. In the great majority of cases of pernicious fever the parasites are numerous in the circulating blood; and, even in æstivo-autumnal

fever, the number of parasites in the peripheral circulation is generally a fair index of the severity of the infection. But this does not always hold. I have recently seen a case of pernicious malaria where death occurred during my visit, in which the number of parasites in the peripheral circulation was moderate—a parasite perhaps in every tenth field. There was, however, a moderate number of characteristic macrophages, containing large masses of pigment, cells rarely seen excepting in very severe infections.

In all cases of doubt it is wise not to rely entirely upon examinations of the fresh blood. While examination of the fresh specimen is usually the most satisfactory method of studying the blood, it must be acknowledged that the small hyaline forms of the malarial parasites are only to be recognized by an individual who is thoroughly familiar with the examination of fresh blood in normal and pathological conditions. The unskilled observer is sure to be confused by the vacuolization and decolorization of the red corpuscles so common, particularly in certain febrile and anæmic conditions. In such cases it is better to resort to dried specimens stained by Romanovsky's method.\* Any one who has studied fresh

\* In connection with these remarks it may be well to quote Lazear's (Johns Hopkins Hospital Reports, 1901, Vol. X, 1), description of his method of preparing Nocht's modification of Romanovsky's stain. The eosin, which gives the best results is that from the Höchst factory, either A. G. or B. A. If prepared by the following method all good methylene blues give satisfactory results. "Polychrome methylene blue is carefully neutralized. This is done by first adding dilute acetic acid until the solution is acid. When litmus paper is dipped into the solution, it is colored by the methylene blue, but on the margin of the moist portion the acidity causes a red line to appear. The solution is now brought back to the neutral point by the addition of more polychrome methylene blue until the red line fails to appear on the blue litmus paper. The polychrome methylene blue may be obtained already prepared. It can, however, be readily made by heating for several hours, on a water-bath, a solution consisting of—

Methylene blue .....	1 part.
Caustic soda .....	1 part.
Water (distilled) .....	100 parts
After cooling, the solution is to be filtered.	

To this polychrome methylene blue an equal quantity of distilled water is added, and then, a saturated solution of ordinary methylene blue, until the red color is completely lost, the solution appearing simply blue. For this purpose about one part of the saturated aqueous solution to ten parts of the diluted polychrome solution will be used.

A solution of eosin is now prepared, according to Nocht, by adding three or four drops of a one per cent aqueous solution of eosin to one or two cc. of water. This is practically a 0.2 per cent solution; it can be made up in quantity. To three or four cc. of the eosin solution, Nocht adds the methylene blue solution until the red color disappears. At this point a fine precipitate is thrown down, and a scum begins to form on the surface.

I found it more satisfactory to keep the two solutions in burettes, as is done by Bastianelli and Bignami. The solutions may be made in large quantity, and the proper proportions in which they should be mixed may be determined once for all

specimens and later examined dried cover-glass smears prepared by this method, will acknowledge that the stained parasites are much more readily picked out than the delicate hyaline bodies in the fresh blood. It is probable that, in a case like that before us, an occasional parasite would have been demonstrable by this method.

(3) An important point in connection with this case is the striking proof afforded by the chart of the therapeutic value of quinine. Few things are more impressive than the instantaneous and specific effect of quinine as observed in a case of this nature. And in connection with such a chart it is perhaps fitting to emphasize again the fact that quinine is a true specific—that wherever one may meet with a case of continued fever, no matter in what part of the world, if the vigorous use of quinine be followed by no definite break in the temperature curve, the case is *not malarial*. It has been definitely proved that continued fevers which resist quinine are due to other causes. The diagnoses of "Simple continued fever" and of "Typho-malarial fever," which were once so common in this very town, and are still, alas, only too frequent in certain parts of our country, all melt away before accurate laboratory methods, and resolve themselves generally into plain typhoid fever.

#### DISCUSSION.

DR. McCRAE.—It is very often a debated question when one has overlooked a condition whether one prefers not to have considered the possibility of it or prefers to remember

by a few experiments. The methylene-blue solution varies a great deal in the amount of the unknown nucleus-staining material which it may contain. One solution may require three parts of the eosin solution to each part of the methylene blue, while another, made in the same manner, may require only one part of the eosin solution to three parts of the methylene blue. When the proper proportion is once determined for a given solution, it remains constant.

The eosin and methylene blue solutions should be mixed immediately before use, and the mixture used only once. When kept a day or two, such a mixture may sometimes give the chromatin stain, but always feebly.

Nocht fixed the blood-smears by placing them in equal parts of absolute alcohol and ether, but I obtained my best results by treating with a one-fourth per cent solution of formalin in 95 per cent alcohol, for one or two minutes. The formalin may be kept in 10 per cent aqueous solution, four or five drops of this being added to 10 cc. of 95 per cent alcohol, just before using.

Before placing the specimen in the staining solution, the scum should be carefully removed by means of filter paper. It is best to use a staining-dish with concave bottom, placing the cover-slip on the bottom with the preparation side down. The specimen is left in the stain for from three to twenty-four hours. The scum should be carefully removed before taking out the cover-glass, as it tends to adhere to the specimen if it comes in contact with it, making the examination difficult or impossible."

The hyaline forms of the parasite appear as delicate blue rings. The central part of the parasite is occupied by a large colorless nucleus, at one side of which is a small spot of chromatin substance which takes a deep carmine violet stain.

that it was considered and discarded. The way the temperature fell after admission made us think it was one of febricula. With the onset of sudden chill and fever we at once thought of malaria and felt no doubt that we had overlooked that cause at first but repeated examinations of the blood were negative. The patient had definite signs at one apex, there was the continued fever with repeated sweats and she was going down hill very rapidly, so that I personally thought the case one of tuberculosis, although no tubercle bacilli could be found. It is a reproach often brought against the profession south of Mason and Dixon's line, that in tuberculosis time is often lost by treatment for malaria, and I suppose it is only fair that we should now have a chance to check up a case on the other side. I did think very decidedly that the case was one of tuberculosis of the lungs with secondary involvement of the peritoneum as the cause of the abdominal pain.

DR. HURD.—I think it unwise to make a diagnosis of febricula in the light of an experience of a physician who had the care of a patient at a summer resort in Canada with a moderate temperature for 10 days. He feared typhoid fever, but as the temperature only lasted 10 days and the patient seemed to get well he thought he had to do with a febricula. He repeated the Widal test from time to time and eventually, after 40 days, the reaction was secured showing that the case had been one of typhoid after all.

#### Nervous Manifestations of Pernicious Anæmia. DR. McCRAE.

Out of 50 cases of pernicious anæmia in the hospital about 20 have shown nervous manifestations of one kind or another. I have gone over the cases with the view of classifying the nervous symptoms but without determining any definite groups. We have at one end of the series the merely sensory disturbances and at the other end complete paraplegia with loss of control of bladder and rectum. The three cases to be presented are examples of different types.

CASE 1. The first patient is a woman, aged 38, who has probably had anæmia for less than a year. She is an example of the minor manifestations of nervous symptoms, merely numbness and tingling. Her blood on admission showed 1,500,000 red cells and they have now risen to 2,500,000.

CASE 2. A very robust looking individual, but you probably noticed as he walked up that his gait is somewhat shuffling. He complains of pain about the hands and feet and a curious feeling of the hand, being very thick and constantly numb. The reflexes are rather exaggerated, his blood count now is almost normal with hemoglobin of 70 per cent. His condition is one of sensory disturbance with marked spastic condition.

CASE 3. This patient complained at the onset only of some tingling with pain in the legs and weakness. His reflexes were gone; he had difficulty in walking, and there was fairly persistent tingling with pain.

Now you see these three cases show different features and that is fairly characteristic of all our series. I think the

predominating type has been that of the second case; a spastic condition with marked sensory disturbance. One may regard these nervous manifestations clinically under three headings. First, there are cases that during life show no symptoms but changes are found in the cord post mortem. Most of the cases where the blood count has gone very low show these cord changes. In the second group the nervous manifestations are secondary, as in the two first cases you saw and probably in the third. The third group are those in which the nervous manifestations come on first and the anamia follows secondarily. I have felt that possibly in regard to the last that they are instances in which the blood condition had not been recognized in the early stage. A fourth group might be added in which certain nervous conditions appear primarily and associated not with primary anamia but with secondary anamia. We have seen no case of the kind here.

To speak briefly regarding the pathologic findings in these cases, they practically all show involvement of the posterior column and a few show also involvement of the lateral columns as well. The cervical region curiously enough usually suffers more than others, and as one goes down the cord the process is less marked. Since improvement occurs in the nervous symptoms as the blood improves, I am inclined to think that the anamia is at the bottom of the cord changes and not that the two conditions are due to the same cause.

#### **Exhibition of Patient and Report of a Case. DR. HUNNER.**

The patient before you is a Bohemian woman, 63 years old. She entered the hospital 28 days ago with a very large cystic feeling abdominal tumor, which we diagnosed as an ovarian cyst. She had noticed the tumor five months but had suffered no symptoms until the past five weeks, during which time there had been considerable abdominal pain on the left side. Two weeks before admission she vomited during a severe attack of pain. Having made a diagnosis of an ovarian cyst with probable malignant degeneration, we made a large incision, extending from a point four centimeters above the umbilicus to the symphysis, intending to remove the tumor without evacuation of its contents. On exposure the tumor was found to be covered by a thin veil of omentum; and hanging from its lower border was an omentum of about normal size, with many rounded and ovoid nodules along its distal edge resembling glandular metastases. We at once decided that unless the tumor could be easily removed we would give up the operation. To determine this point the tumor was rolled out of the cavity when it was seen to arise from the region of the transverse colon and to have no pelvic attachments. The transverse colon was closely attached across the under surface of the tumor and it could not be determined whether this tumor arose from the bowel wall, the mesocolon, or the omentum. The splenic end of the transverse colon dipped directly posteriorly from the tumor and was firmly fixed to the posterior abdominal wall. The hepatic flexure, however, was freely movable and gave promise of being easily carried across the cavity to meet the splenic

end. No glandular enlargements could be detected in the mesocolon or above.

Enucleation was begun by separating the tumor from the stomach, the bridge of omentum connecting the two bodies requiring about a dozen catgut sutures for its many large vessels. The portions of omentum springing from the hepatic and splenic flexures and meeting the tumor on its sides were next tied off and cut. This left only the vessels of the transverse mesocolon to be dealt with. By raising the tumor and allowing light transmission one could easily determine the circulation of the bowel and the best points for resection on either side of the tumor. Heavy artery clamps were placed on the tumor side of the points for resection, the mesenteric circulation was ligated, and, after placing pre-section sutures, the bowel was severed at both hepatic and splenic regions, and the tumor with the attached transverse colon removed. An end-to-end suture without the use of mechanical appliances presented no difficulties except for the very short fixed splenic end.

A Mitchell-Hunner mesenteric suture was placed, and then the two sides of the anastomosis were successively built up by first bringing the mucosa coat end to end with a fine catgut whipped suture, and immediately over each of these sutures the other coats were approximated by a mattress suture of fine silk. A row of intermediate mattress sutures of silk finished the anastomosis in a secure manner. A running catgut suture closed the A-shaped space in the transverse mesocolon. A small gauze wick was introduced through the upper end of the abdominal wound and carried down to the site of anastomosis. The entire operation from incision to closure occupied two hours and fifteen minutes. The patient had lost practically no blood and left the table with a pulse of 96.

She made a rapid recovery without special event until the twenty-first day, when, after walking about the ward, she complained of pain and tenderness in the popliteal space of the right leg. Fearing phlebitis we kept her in bed with the leg elevated for the next two days, when all symptoms had disappeared. She is now walking about and ready to go home.

The tumor, as you see, is of the solid variety with many areas of cystic degeneration and necrosis. On removal it measured about 30 cm. in diameter. It rested upon the transverse colon and was attached for several centimeters to the transverse mesocolon. The tumor surface between the mesocolon and the stomach is covered by a layer of omentum, so it is impossible to say whether the tumor arises from the mesocolon or from the omentum.

Since hardening the specimen it is readily seen that the tumor has no organic connection with the bowel.

A more minute pathological report will be made later, but on hurried microscopical examination the tumor seems to be sarcoma.

**Gonorrhoeal Endocarditis, Exhibition of Specimens. DRs.**

HARRIS AND JOHNSTON.

(To be published later.)

## SUMMARIES OR TITLES OF PAPERS BY MEMBERS OF THE HOSPITAL AND MEDICAL SCHOOL STAFF APPEARING ELSEWHERE THAN IN THE BULLETIN.

- SAMUEL AMBERG, M. D. An Unusual Case of Spasmus Nutans.—*Archives of Pediatrics*, November, 1901.
- CHARLES RUSSELL BARDEEN, M. D., and WARREN HARMON LEWIS, M. D. Development of the Limbs, Body-Wall and Back in Man.—*American Journal of Anatomy*, 1901, Vol. I, No. 1.
- LEWELLYS F. BARKER, M. D. On the Clinical Aspects of Plague.—*American Journal of the Medical Sciences*, October, 1901.
- JOSEPH C. BLOODGOOD, M. D. Blood Examinations as an Aid to Surgical Diagnosis.—*Medical News*, August 31, 1901; *Maryland Medical Journal*, September, 1901.
- GEORGE BLUMER, M. D. The Bacteriology of Lobular Pneumonia, especially in adults. *Proceedings of the New York Pathological Society*, March, 1901; also in *Albany Medical Annals*, August, 1901.
- The Bacteriology of Lobular Pneumonia, especially in Adults.—*Albany Medical Annals*, August, 1901.
- The Present Status of the Infectious Theory of Malignant Neoplasms.—*The New York State Journal of Medicine*, November, 1901.
- and ANDREW MACFARLAND, M. D. An Epidemic of Noma; Report of Sixteen Cases.—*American Journal of the Medical Sciences*, November, 1901.
- WILLIAM D. BOOKER, M. D. The Early History of the Summer Diarrhoeas of Infants.—*Archives of Pediatrics*, July, 1901.
- THOMAS R. BROWN, M. D. On the Treatment of Tetanus, with Report of a Case that Recovered under Symptomatic Treatment Alone.—*Journal of the Alumni Association of the College of Physicians and Surgeons*, Baltimore, July, 1901.
- The Diagnosis, Aetiology, Prophylaxis, and Treatment of Cystitis, Pyelitis, and Pyelonephritis in Women.—*New York Medical Journal*, August 31, 1901.
- The Practical Value of Blood Examination in Medicine and Surgery.—*American Medicine*, October 19, 1901.
- H. WARREN BUCKLER, M. D. Care of the Indigent Tuberculous.—*Maryland Medical Journal*, August, 1901.
- HARVEY CUSHING, M. D. Concerning the Poisonous Effect of Pure Sodium Chloride Solutions upon the Nerve-Muscle Preparation.—*American Journal of Physiology*, October 1, 1901.
- Haller and His Native Town.—*American Medicine*, October 5 and 12, 1901.
- JOSEPH ERLANGER, M. D. and ALBION WALTER HEWLETT, M. D. A Study of the Metabolism in Dogs with Shortened Small Intestines.—*The American Journal of Physiology*, September 1, 1901.
- JOHN M. T. FINNEY, M. D. Anaesthetics in Heart Disease.—*American Journal of the Medical Sciences*, August, 1901.
- and LOUIS P. HAMBURGER, M. D. The Relation of Appendicitis to Infectious Diseases.—*American Medicine*, December 14, 1901.
- SIMON FLEXNER, M. D. A Comparative Study of Dysenteric Bacilli.—*Centralblatt für Bakteriologie Parasitenkunde und Infektionskrankheiten*, Bd. 30, No. 12.
- The Pathology of Bubonic Plague.—*American Journal of the Medical Sciences*, October, 1901.
- W. W. FORD, M. D. Classification of Intestinal Bacteria.—*Journal of Medical Research*, Vol. 1, No. 1.
- THOMAS B. FUTCHER, M. D. Fusel-Oil Poisoning, with Special Reference to the Copper-Reducing Substances Eliminated in the Urine.—*American Medicine*, August 10, 1901.
- Cirrhosis with Pigmentation.—*The Journal of the American Medical Association*, September 28, 1901.
- NORMAN McLEOD HARRIS, M. D. and WARFIELD T. LONGCOPE, M. D. Micrococcus Zymogenes: Some Additional Observations upon its Occurrence.—*Centralblatt für Bakteriologie, Parasitenkunde und Infektionskrankheiten*. Erste Abt. Bd. 30, No. 9.
- AUGUST HOCH, M. D. On Certain Studies with the Ergograph.—*The Journal of Nervous and Mental Disease*, November, 1901.
- WILLIAM H. HOWELL, M. D. and C. E. BRUSH, JR. A Critical Note upon Clinical Methods of Measuring Blood Pressure.—*Boston Medical and Surgical Journal*, Aug. 8, 1901.
- HENRY BARTON JACOBS, M. D. The Treatment of Consumption in Local Sanatoria.—*Maryland Medical Journal*, December, 1901.
- WALTER JONES, M. D. and JOHN AUER. On the Oxidation of Native Pigments.—*The American Journal of Physiology*, 1901, Vol. V, No. 6.
- HOWARD A. KELLY, M. D. Scratch-Marks on the Wax-tipped Catheter as a Means of Determining the Presence of Stone in the Kidney and in the Ureter.—*The American Journal of Obstetrics*, October, 1901.
- IRVING PHILLIPS LYON, M. D. The Clinical Study of the Blood. A Brief Guide to the Application of Blood Examination to Medicine and Surgery. Reprinted from *Gaylord and Aschoff's Principles of Pathological Histology*, American Edition, 1901, being Chapter XVIII. Illustrated with one colored lithographic plate, one heliotype plate, and four wood-cuts.
- This is one of the briefest (35 pages), yet most complete chapters on the principles and application of blood examina-

tion to clinical medicine and surgery, that has appeared in any general text-book. The first half of the paper is devoted, to a description of the various elements of the blood, the methods and technique of examination, and the general facts and principles of the physiology and pathology of the blood in health and disease. The second part of the paper treats of the special pathology of the blood and describes in the briefest form consistent with clearness the blood picture in nearly two hundred different morbid affections, arranged in alphabetical order, with special notes under each disease on differential diagnosis. References to the literature are given in footnotes.

Blood Examination Applied to Surgery. Reprinted from *Park's Surgery by American Authors*. Third Edition, 1901, being Chapter III.

A brief chapter (13 pages) written to supply the surgeon with practical data on the value of blood examination for diagnosis and prognosis in surgical affections. The general principles and facts of blood examination are first elucidated in a systematic manner and then the application of these principles to special morbid processes of surgical interest is described in a limited number of surgical affections.

— and CHARLES CARY, M. D. Pseudomembranous Inflammation of the Mucous Membranes Caused by the Pneumococcus. Review of the Literature and Report of a Case of Pneumococcic Pseudomembranous Exudation on the Mucous Membranes of the Mouth, Tongue, Throat, Nose, Eyes, Glans Penis, Anus, etc., Complicating Acute Lobar Pneumonia.—*Transactions of the Association of American Physicians*, Vol. XVI, 1901; and *The American Journal of the Medical Sciences*, October, 1901.

Summary of case: Acute lobar pneumonia of both bases, with development during the first ten days of a profuse pseudomembranous exudate, first upon the tonsils and quickly extending to the mucous membranes of the lips, tongue, mouth, palate, throat, and nose and transferred to the eyes, glans penis, and anus; physical signs of fibrinous pleuritis; marked and persistent tympanites; membranous shreds and mucus in the stools. Microscopic examination: bacillus diphtherie, streptococcus, saccharomyces albicans, etc., absent; diplococcus pneumoniae present in abundance in the sputum and in the exudate from all locations, grown in cultures and injected into a rabbit and recovered from the organs and blood after death. Diagnosis: pneumococcic infection resulting in acute pneumonia, pleurisy, and fibrinous exudation upon the mucous membranes.

The literature of pneumococcic pseudomembranous inflammation of the mucous membranes is reviewed and many cases cited, under the following divisions:

1. *Cases of Pseudomembranous Inflammation of Mucous Membranes Occurring in Association with Pneumonia*. This class includes (a) cases in which the pneumococcic origin of the croupous exudate upon the mucous membranes was not proved, but merely suggested by its association with pneumonia, and (b) cases in which the pneumococcus was shown by bacteriologic methods to be the specific agent in producing the lesion.

II. *Cases of Pseudomembranous Inflammation of Mucous Membranes of Pneumococcic Origin, Independent of Pneumonia*. The involvement of the various mucous membranes of the body in a pseudomembranous process caused by the local action of the pneumococcus is probably less infrequent than would be inferred from the almost total absence of mention of such a process in the text-books. The course of such cases is usually favorable.

— Cancer Distribution and Statistics in Buffalo for the Period 1880-1899, with Reference to the Parasitic Theory.—*Third Annual Report of the New York State Pathological Laboratory of the University of Buffalo*, for the year 1900. Albany, N. Y., 1901.

The statistical method is adopted in this study, following up the suggestive findings of Behla at Luckau, in Germany. The main purpose was to find whether there occurred in the city of Buffalo any local foci of the disease in special regions of the city or in certain houses, out of proportion to the population of such places, and in case such foci occurred, what relation existed between them and their natural environments and the conditions of race, social status, and habits of the population. The statistics were collected from the original official certificates of death, signed in each case by a physician, preserved as the mortality records of the board of health of the city of Buffalo. All non-resident cases were excluded. The statistics embraced 2299 cases occurring during the twenty years, 1880-1899. The residence of each of these cases is indicated on a large (4 by 3 feet) street map of the city by colored dots. The results of the investigation are presented under the following headings: 1.) House Distribution as shown on the City Map. 2.) Multiple-case houses ("Cancer Houses"). 3.) Increasing Cancer Rate. 4.) Race Distribution. 5.) Age Distribution. 6.) Sex Distribution. 7.) Anatomical Distribution.

Some of the more important results of this study are briefly indicated in the following summary:

(1) The house distribution of cancer on the map shows an area of marked concentration in the German wards. No other relation than that of race can be determined to exist between this area of concentration and local conditions.

(2) That there is a real relation between this local concentration and race (German) is further indicated by the race table, which shows that cancer is many times more frequent among the foreign-born and particularly the Germans than the native-born. The latter fact is also verified by the United States census for 28 large cities. The cancer rate of foreigners, in general, was 4.59 times the rate for the native-born and the corresponding rate for Germans (and Poles) was 4.81.

(3) The Germans (and Poles) were further specially distinguished from other classes by the high rate (43.8 per cent.) of involvement of the stomach, 2.08 times the rate (21 per cent.) shown by the native born. Cancer of the stomach, therefore, was ten times more frequent in the Germans (and Poles) than in the native-born in Buffalo, for equal numbers of each. Such high figures seem hard to explain on the embryonic or irritation theories and tend to support the parasite theory of cancer, by supposing that the peculiar diet of the Germans is more liable to contamination with a parasite of cancer than the more ordinary diet of other classes. Cancer of the uterus and breast in Germans (and Poles) was correspondingly low, being hardly more than half as frequent as in the native-born. This fact seems to be a further argument for the parasitic as opposed to the embryonic or irritation theories, considering the fact that the birth rate and the habit of nursing at the breast (conditions predisposing to degeneration of these organs) are greater among Germans than native-born women.

(4) The ratio of males to females, the latter taken as 100, was 93 for Germans (and Poles) and from 51 (native-born) to 61 (all Europeans except Germans and Poles) for all other races and classes. The high German male rate is probably directly dependent upon the high rate of cancer of the stomach (especially in males) and the low rate of cancer of the uterus

and breast (females) found to characterize the Germans as opposed to other races.

For all classes the ratio of males to females was found to have risen during the twenty years covered by the investigation. This rise was very slight for the native-born.

(5) An increase in the general cancer rate from 32 to 53 per 100,000 of population (65 per cent.) took place from 1880 to 1899. A similar increase has been shown in all countries. This increase is thought to be partly real and not entirely apparent. The rate of increase is shown to depend in part at least upon changes in the proportion of the foreign-born, as the cancer rate in the foreign-born is so much higher than in the native-born.

In conclusion the writer notes the sources of unavoidable error in the statistical method of investigation and advises caution in making deductions. Conclusions can be accepted only after repeated and thorough confirmation, and until then all generalizations should be avoided or treated merely as suggestive possibilities that may stimulate to further investigation.

W. G. MACCALLUM, M. D. A Case of Multiple Myeloma.—*The Journal of Experimental Medicine*, 1901. Vol. VI, No. 1.

— and S. S. BUCKLEY, V. S. Acute Epizootic Leucoencephalitis in Horses.—*The Journal of Experimental Medicine*, 1901. Vol. VI, No. 1.

JOHN N. MACKENZIE, M. D. The Study of Laryngology in the University and in the Higher Medical Education.—*Journal of the American Medical Association*, July 20, 1901.

EUGENE L. OPIE, M. D. Filarial Lymphatic Varix.—*American Journal of the Medical Sciences*, September, 1901.

WILLIAM OSLER, M. D. On the Advantages of a Trace of Albumin and a Few Tube Casts in the Urine of Certain Men Above Fifty Years of Age.—*New York Medical Journal*, November 23, 1901.

J. HALL PLEASANTS, M. D. Bacteriological Diagnosis of Typhoid Fever from a Clinical Standpoint.—*Journal of the Alumni Association of the College of Physicians and Surgeons*, Baltimore, July, 1901.

OTTO G. RAMSAY, M. D. A Case of Congenital Malformation of the Female Generative Organs.—*Yale Medical Journal*, December, 1901.

ROBERT L. RANDOLPH, M. D. Double Suppurative Irido-Choroiditis in Association with Purpura Hemorrhagica.—*Archives of Ophthalmology*, 1901, Vol. 30, No. 4.

— Herpes Zoster Ophthalmicus Resulting in Loss of the Eye.—*Archives of Ophthalmology*, 1901, Vol. 30, No. 4.

HUNTER ROBB, M. D. The Advantages and Disadvantages of Drainage after Abdominal Operations.—*Annals of Gynecology and Pediatrics*, September, 1901.

— Two Cases of Brain Tumor in Gynecological Practice.—*The American Journal of Obstetrics*, October, 1901.

J. ERNEST STOKES, M. D. The Importance of an Early, Definite Diagnosis of Appendicitis.—*The Carolina Medical Journal*, June, 1901.

WILLIAM SYDNEY THAYER, M. D. Observations on the Frequency and Diagnosis of the Flint Murmur in Aortic Insufficiency.—*American Journal of the Medical Sciences*, November, 1901.

— On the Occurrence of Strongyloides Intestinalis in the United States.—*The Journal of Experimental Medicine*, 1901, Vol. VI, No. 1.

SAMUEL THEOBALD, M. D. The Evolution of the Ophthalmoscope and what it has done for Medicine.—*Transactions of the Medical and Chirurgical Faculty of the State of Maryland*, April, 1901.

Abstract of an address delivered before the Medical and Chirurgical Faculty of Maryland at the opening of its one hundred and third annual session, and published in full in the *New York Medical Journal* for June 22, 1901.

The selection of the theme was suggested by the fact that the year 1901 is the fiftieth anniversary of the invention of the ophthalmoscope by Helmholtz. By way of introduction, a brief resumé is given of the investigations regarding the luminosity of the eyes of certain animals, and of the human eye under certain conditions, by Prévost, Rudolphi and Behr and, at a later period, by Cumming and Brücke, of which Helmholtz's invention seemed but the logical outcome. Of these investigators Cumming was the only one who had in view the discovery of a method of detecting pathological changes in the interior of the eye.

The contrivance of an ophthalmoscope, by scraping off a little of the silvering from the back of a plain mirror which was set obliquely in a suitable tube, by Charles Babbage, F. R. S., in 1847, four years before Helmholtz's invention, "was an event of much interest in the history of ophthalmoscopy, though it had no bearing upon Helmholtz's invention and exerted absolutely no influence upon the subsequent evolution of the ophthalmoscope." Through the failure of Wharton Jones, to whom Babbage submitted his invention, to appreciate its value, it attracted no attention, and, in fact, was wholly lost sight of until after Helmholtz described his instrument; nevertheless, the credit of being the inventor of the first ophthalmoscope is undoubtedly due to Babbage. It is a remarkable fact that in not one of the numerous biographical sketches of Charles Babbage, who was most widely known through his efforts to construct a calculating machine, and who, in his later years, gained great notoriety because of his "fierce hostility" to organ-grinders, is there the slightest reference to his having invented an ophthalmoscope.

Helmholtz's ophthalmoscope was unquestionably the legitimate parent of all later ophthalmoscopes; it was also the first instrument with which the background of the living eye was seen *distinctly*. Furthermore, Helmholtz was absolutely the first to suggest the *indirect* method of ophthalmoscopy (though the credit for this is commonly given to Ruete); and it was he who directed the world's attention to the subject. Still, what was essential in his ophthalmoscope—the plain glass reflector—was not wholly original, having been but the practical application of von Erlach's observation that the light reflected from his spectacle lenses at times caused the pupils of persons in front of him to emit an unusual glow; and what was original—the insertion of a concave lens between the reflector and the eye of the observer—was "distinctly not essential" and was moreover, "the outcome of a misconception—a fortunate misconception, as it turned out—upon his part."

The employment of this concave "ocular," was the result of Helmholtz's belief that the eye under examination would tend

to focus for the image of the nearby flame, and hence that the light reflected from its fundus would leave the cornea in converging rays, which must needs be rendered parallel or divergent in order to afford clear vision to the observing eye. As a matter of fact, the observed eye shows but little inclination to employ its focussing power, especially in the direct method of examination which Helmholtz chiefly relied upon. On the other hand, in this method particularly, the beginner in the use of the ophthalmoscope finds it very difficult to relax his accommodation or to focus for other than divergent rays of light, and is, therefore, greatly helped by employing a concave lens. Thus it came about that the concave lens used by Helmholtz, though it was not an essential feature of a successful ophthalmoscope, and was employed by him to meet an unreal difficulty, was, nevertheless, of the greatest assistance to him and his earlier pupils, who were, of course, all neophytes in ophthalmoscopy.

Within a few months after Helmholtz announced his invention, Epkens, an instrument-maker of Amsterdam, constructed an ophthalmoscope in which a plane mirror, with the silvering removed from a small space in its center, was substituted for the less efficient glass plates used by Helmholtz, this being essentially a return to the earlier instrument of Babbage. A still more decided advance was made by Professor Ruete, of Göttingen, who, in 1852, suggested the employment of a *concave* mirror in place of the plane mirror of Epkens, and thus made indirect ophthalmoscopy, the value of which he was the first to appreciate, practicable. It is worthy of remark that, although the subsequent evolution of the ophthalmoscope was almost wholly the work of ophthalmologists, they took no part in the scientific observations which led to its invention, and had no hand in the invention itself or in the improvements made in it up to the time of Ruete.

The adaptation of the ophthalmoscope to accurate optometry to the measurement of the refraction of the eye, constitutes the next decided step in its evolution, and here American ophthalmologists come definitely to the fore, the largest measure of credit being due to the late Dr. Edward G. Loring, of New York, for bringing the refracting ophthalmoscope to its present state of perfection. The ophthalmoscope of Mr. Morton, of London, is, perhaps, the strongest rival of the perfected instrument of Loring, with its tilting mirror, revolving quadrant, etc., but is hardly its equal, though it has undoubted merits.

As usually happens under such circumstances, when the ophthalmoscope was first brought to the world's attention by Helmholtz, much skepticism was shown as to its real value, and it was contended that its employment, even for a few moments, would be "highly injurious," and that the knowledge gained from it would be more than offset by the harm it was likely to do. However, in spite of such pessimistic prognostications, it grew in favor rapidly, and soon came to be appreciated at its true worth. Among the first to recognize its value and acquire skill in its use were Von Graefe and Liebreich, in Germany; Donders, in Holland; Jaeger, in Austria; Desmarres

and Sichel, in France; Bowman and Hulke, in England, and E. Williams, of Cincinnati, in this country. These names one is not surprised to find connected with the early history of ophthalmoscopy; but one hardly expects to be told, as Clifford Allbutt tells us in the introduction to his work on *The Ophthalmoscope*, that Mr. Spencer Wells was among the first in England (in an article in the Medical Times for September 10, 1853) to insist upon the great value of the ophthalmoscope in diseases of the eye; or to learn, from a comprehensive and interesting account of the earlier ophthalmoscope by the late Dr. Christopher Johnston, published in The Transactions of the Medical and Chirurgical Faculty of Maryland, in 1854, that Dr. George W. Miltenberger, whose name we associate with a very different branch of medicine, had already, at that early period, acquired proficiency in the use of the ophthalmoscope.

To comprehend the veritable revolution which the invention of the ophthalmoscope brought about in ophthalmology, one needs but to glance over the table of contents of any of the standard works upon diseases of the eye published prior to this period, and note the varieties and sub-varieties of "amaurosis" which are enumerated, the causes assigned for it and the remedial measures suggested to combat it. Ophthalmology deprived to-day of the ophthalmoscope might be likened to a rudderless ship; but a ship bereft, at once, of compass and sextant and rudder as well, would seem to afford a still more apt comparison.

But ophthalmology is not the only department of medicine that is beholden to the ophthalmoscope. The specialists in diseases of the eye had hardly earned its value before his brethren interested in affections of the brain and nervous system began to realize how great a boon it was to them as well. Hughlings Jackson, in London, and Clifford Allbutt, in Leeds, were the first to approach the subject from the standpoint of the neurologist, and they may well be called the fathers of medical ophthalmoscopy. Their labors have been well supplemented by another English worker in this same field, Dr. W. R. Gowers. Besides affections of the brain and nervous system there are many other maladies, such as Bright's disease, diabetes, pernicious anemia, leucocythemia, angio-sclerosis, etc., in which intraocular changes, more or less characteristic and hence of diagnostic value, are revealed by the ophthalmoscope.

WILLIAM HENRY WELCH, M. D. The Relation of Yale to Medicine.—*Yale Medical Journal*, November, 1901.

J. WHITRIDGE WILLIAMS, M. D. Pelvic Indications for the Performance of Cesarean Section.—*American Medicine*, September 28, 1901.

HUGH H. YOUNG, M. D. Chronic Cystitis Due to Bacillus Typhosus—Report of a Case of Seven Years' Duration.—*Maryland Medical Journal*, November, 1901.

— Genital Tuberculosis, with Special Reference to the Seminal Vesicles.—*Annals of Surgery*, November, 1901.

## THE JOHNS HOPKINS HOSPITAL BULLETIN.

The Hospital Bulletin contains details of hospital and dispensary practice, abstracts of papers read, and other proceedings of the Medical Society of the Hospital, reports of lectures, and other matters of general interest in connection with the work of the Hospital. It is issued monthly.

Volume XII is now completed. The subscription price is \$1.00 per year. The set of twelve volumes will be sold for \$23.00.

## NOTES ON NEW BOOKS.

**Operative and Practical Surgery for the Use of Students and Practitioners.** By THOMAS CARWARDINE, M.S. (Lond.), F. R. C. S., Assistant Surgeon Bristol Royal Infirmary, with 550 illustrations most of which are original drawings by the author. (Bristol: John Wright & Co., 1901.)

This manual of 661 pages is intended to give students and practitioners the essentials of operative and practical surgery, as the writer tells us in his preface. A careful examination of the book seems to indicate that he has accomplished his purpose very well. While in so small a compass only a very concise and often incomplete discussion of the subjects under consideration can be given, the book on the whole is quite satisfactory. There are, however, numerous points which might be improved upon specially for the use of American students. In the present stage of medical education when every student is supposed to own a special book on gynaecology and on diseases of the eye and ear it seems out of place to introduce a discussion of these subjects when the space might be better taken up with a more complete discussion of general surgical topics. In a text-book the consideration of methods of extracting teeth also seems out of place as such work is almost universally turned over to dentists in this country at least. In the general considerations on technique we find antiseptic treatment advocated practically to the exclusion of aseptic technique, quite contrary to the general views of most American surgeons. We regret to find that the writer believes that the use of gloves is unnecessary and cumbersome. In the treatment of fractures numerous splints are depicted and are advised for the ordinary fractures of the leg, while the more simple and effectual method by use of plaster of Paris casts, is not even mentioned. In the chapter on brain surgery, the technique of trephining is described, but the osteoplastic flap which is now generally considered the best method of opening the skull is not even mentioned. In the chapter on the surgery of the chest, a description is given of the method of opening the pleural cavity for empyema without the removal of a rib, a method which we believe to be unsafe and unsurgical. In discussing the treatment of hydrocele the various methods of tapping with injection, excision of a part of the sac and drainage, and complete excision are all described without any statement as to the comparative merits of the various procedures or their adaptability to individual cases. We notice the same fault in connection with many other operations. While these and some other points might be criticized, in many other respects the book is most excellent. The illustrations are as a rule, simple and very good. Most modern surgical procedures are at least mentioned and usually the best methods are adequately described. On the whole the text-book is as satisfactory as most of those which come into the hands of students, although as we have suggested, some changes would be desirable to adapt the book to use in American medical schools.

**A Text-Book of the Practice of Medicine.** By JAMES M. ANDERS, M.D. Fifth edition. (Philadelphia and London: W. B. Saunders & Co., 1901.)

As the previous edition of this text-book was carefully reviewed about a year ago, there is little additional to say regarding this one. Dr. Anders has made changes wherever the research work of the past year has rendered them necessary and he is to be complimented on the general thoroughness with which changes and additions have been made.

**A Manual of Determinative Bacteriology.** By FREDERICK D. CHESTER, Bacteriologist of the Delaware College Agricultural Experiment Station, etc., etc. (New York: The Mac-Millan Co., 1901.)

With the aim to facilitate identification of bacteria and to bring before the minds of workers in bacteriology the principles underlying scientific nomenclature, the author has performed a worthy service in his excellently compiled book.

The title well indicates the chief scope and object of the work, and he who carefully reads through the pages will, even though he take issue with the author now and then, find sufficient to highly praise.

Chapter I deals with the general morphology of bacteria in a clear, concise manner.

In Chapter II, the author gives a good resumé of cultural and biochemical characters, and draws attention to the present day fashion of descriptive verbosity, successfully demonstrating what a few well-chosen words can do in clearly and concisely describing all conditions as they are found. Here might be mentioned, a little out of place, possibly the existence of a glossary of terms at the end of the book which will be found of great assistance in attempting description of a species.

In discussing the preparation of media the author follows the scheme, as laid down for such, by the Bacteriological Committee of the American Public Health Association, a point not as yet sufficiently emphasized by American authors.

Chapter III. This is the writer's *pièce de résistance*. The opening pages treat of the relation of bacteria to other organic forms of life; the classification of them into families; the laws of nomenclature; and, to facilitate study, the arrangement of the species into groups.

In the main, the classification and definitive terms of Migula have been followed, although, in dealing with the tubercle bacillus and other branching forms the writer favors those of Lehmann and Neumann.

Much time and labor have evidently been expended upon the grouping of the species, and the result as a whole is satisfactory, but it is difficult to understand the reasons for placing *B. zenkeri* and *B. zopfii* in the group of bacteria forming endospores, and why such organisms as *Bact. bordonii*, *Bact. crassum* and *Bact. rhinoscleromatis* have been removed from the Friedländer group.

Typographical errors of omission and commission are occasionally to be noted, such as "spirilli" for "spirilla" (p. 41, sixteenth line from the top), and "rhinosclermatis" for "rhinoscleromatis" (throughout the book), otherwise the typography is pleasing to the eye. A few illustrations are to be found which facilitate the explanations in the text.

The book should be given a cordial reception because it is helpful. And Mr. Chester is deserving of the thanks of the many bacteriologists in this country, for the time, energy and thought expended in rendering clearer much that has been heretofore obscure, and in pointing out the way to a more truly scientific comprehension of facts and principles involved. Nov. 30th 1901. N. MacL. H.

**A System of Physiologic Therapeutics. A Practical Exposition of the Methods, other than Drug-Giving, Useful in the Prevention of Disease and in the Treatment of the Sick.** Edited by SOLOMON SOLIS COHEN, A. M., M. D., Professor of Medicine and Therapeutics in the Philadelphia Polyclinic; Lecturer on Clinical Medicine at Jefferson Medical College; Physician to the Philadelphia Hospital, etc. Volume III—

Climatology, Health Resorts, Mineral Springs. By F. PARKES WEBER, M. A., M. D., F. R. C. P. (Lond.), Physician to the German Hospital, Dalston; Assistant Physician North London Hospital for Consumption, etc. With the Collaboration for America of GUY HINSDALE, A. M., M. D., Secretary of the American Climatological Association, etc. In two books. Book I—Principles of Climatology—Ocean Voyages—Mediterranean, European and British Health Resorts. Book II—Mineral Springs, Therapeutics, etc. Illustrated with Maps. Price for the complete set, \$22.00 net.

These two volumes devoted to the general subject of climatology consist in the aggregate of 700 pages, barring indices. The first 70 pages deal with climate, the air, absolute and relative humidity, barometric pressure and the like. Then in a few pages is discussed the physiological effects of low and high altitude, warm and cold, dry and moist climates. One can but notice a slight degree of scepticism in accepting the mosquito theory of the propagation of malaria, on p. 48: "Malaria, which a generation back was prevalent in certain parts of England has been banished by the drainage of fens and marshes. The prevalent tendency is to explain this by the abolition of favorable breeding places for mosquitoes, in particular those of *Anopheles*, which have been demonstrated to be the intermediate hosts of the plasmodia of malaria. The exclusive rôle of the mosquito as a carrier of malarial infection has not, however, been proved and there may be other factors not yet demonstrated."

Part II covering 487 pages is given up to a description of the health resorts of the whole world. Each country is considered and few towns or cities escape. One naturally turns to see what is said of places with which one is familiar and is disappointed to find how much like those of the ordinary guide books the descriptions are. For instance, "Royat (1480 feet) beautifully situated at the entrance of the Tiretaine Valley is 1½ miles to the west of Clermont-Ferrand with which it is connected by train and electric tramway. The view from Royat over the fertile plain of the Limagne toward the Forez Hills on the east is magnificent. The thermal muriated alkaline springs on whose account Royat has sometimes been called the "French Ems," have a great reputation in chronic gout, rheumatoid arthritis, chronic catarrhal conditions of the respiratory organs, etc. The springs of Royat contain more or less iron, bicarbonate as well as sodium chloride and sodium bicarbonate. Royat is a fashionable spa very much frequented during the season, especially from the middle of June to the middle of August, and the hotel accommodation is first-class."

Turning to the resorts of the United States the book falls open to Long Island, Volume IV, page 100. "Long Island lies south of Connecticut between 72° and 74° west longitude and 41° north latitude. At its western extremity lies a portion of the city of New York—the boroughs of Brooklyn and Queens—separated from Manhattan by the East River and containing over 1,250,000 inhabitants. At the time of its consolidation with New York city, Brooklyn was the fourth city of the United States in population. It is connected with Manhattan by a bridge over which a very large number of Brooklyn residents cross daily to and from their occupation. Other bridges are under construction. At the eastern end of Long Island 120 miles distant, is Montauk Point, used in 1898 as a camp for United States troops at the close of the Spanish-American war. Experience showed, however, that it was not well suited for that purpose. . . . The resorts of Long Island are quickly reached from New York city by rail and the nearer ones by water route and by trolley cars. Some are used principally as summer resorts and others as places of permanent resi-

dence, though these also have a great influx of visitors in the summer. The most accessible resort is Coney Island including Brighton Beach and Manhattan Beach. These are chiefly patronized for a few hours of holiday excursions in the afternoon and evening and provide for thousands of visitors of a somewhat 'mixed' character, a varied entertainment. Next in order on the south shore are the Rockaways, Long Beach, Babylon, Islip, Patchogue, Quogue, the Moriches, Chinnecock Hills, Southampton and Easthampton. Along the sound are Flushing, Little Neck, etc., etc. The chief attractions of all these resorts are the facilities they offer for bathing, boating and fishing. The climate is especially suitable for the neuræsthenic and for general relaxation from business cares."

These two descriptions taken at random, will give a fairly adequate idea of the character of the descriptions of the resorts mentioned. One chapter written by Dr. Titus Munson Coan of New York, is devoted wholly to the Hawaiian Islands. Careful and complete consideration is given to the climate, the winds, the rainfall and temperature of these islands.

For the physician the last part of the second volume devoted to the therapeutic effects of climate is the most valuable portion of the work. Here one finds the subject considered from the standpoint of general and particular diseases. For instance, the kind of climate, altitude etc., useful in gout and gouty conditions. Definite suggestions of value are given, though the tendency is still to such prolixity as to be of little avail to a physician or patient seeking a proper resort. For example, page 285, "The best American resorts for the treatment of gout and allied affections are Hot Springs, North Carolina, Las Vegas Hot Springs, New Mexico, Klamath Hot Springs, California and Mudlavia near Attica, Indiana. At Las Vegas, Klamath and Mudlavia mud baths are employed with great success. Other mineral springs worthy of mention are those at Bedford, Pennsylvania, Ukiah and Santa Ysabel, California, the Poland in Maine, Richfield, New York, the vichy spring at Saratoga, New York, and Buffalo lithia springs, Virginia. There are many other waters of value in the treatment of gout, some such as those of Glen Summit and Minnequa in Pennsylvania, depending like the Poland water on great purity and freedom in use. Others, such as Londonderry lithia, Buffalo lithia, Farmville lithia, depending in part on the contained salts of which lithium compounds are the least important."

In writing any book upon climatology and health resorts the author is necessarily somewhat embarrassed lest he display unwarrantable partiality in his description of single places. Yet in order that a book may be of maximum usefulness definite strong statements are needed. In a notice of volume I of this series in the BULLETIN the following words were used: "It is greatly to be hoped that the completed work will not become so voluminous as to lose its general usefulness." "The appearance of such a system of medicine is timely, as no author or authors have until now gathered together in one volume or series of volumes in English these methods which are so very important in the treatment of disease." To all who have strong feelings that often much more can be accomplished by so-called physiologic therapeutics than by the mere administration of drugs, much was hoped for in this system of Dr. Cohen's. That these volumes which have appeared are of value there can be no doubt, but that they are fulfilling all that was looked for is not true; probably our expectations were too high, perhaps unreasonable but the fear is irresistible that they are becoming too voluminous and diffuse, and that they will be found in medical libraries rather than upon the tables of the every-day practitioner, where they ought to be in order to do their greatest good in bringing about the reform so much needed in our treatment of disease, when every measure likely

to aid nature in the least shall be considered, and our thoughts shall no longer be so completely centred upon the Pharmacopoeia.

A Treatise on the Acute Infectious Exanthemata including Variola, Rubella, Scarlatina, Kibella, Varicella, and Vaccinia, with especial reference to diagnosis and treatment. By WILLIAM THOMAS CORLETT, M.D., L.R.C.P., Lond., Professor of Dermatology and Syphilology in Western Reserve University, etc., octavo, 392 pages. Illustrated by 12 colored plates, 28 half-tone plates from life and 2 engravings. (Philadelphia: F. A. Davis Company, Publishers, 1901.)

The necessary isolation of patients suffering from any one of the exanthemata and the risk of conveying the infection to a third person, render it impossible for the student to have free access to individuals suffering from the various infectious diseases. The vast majority of students are consequently graduated with the most inadequate practical knowledge of the various exanthemata. It was the recognition of this deplorable fact that prompted the author to publish the present volume. The author's excellent lantern-slide reproductions of photographs of the various exanthems are well known to many. The numerous excellent plates from photographs of actual cases, many with the characteristic tints accurately portrayed, undoubtedly add very materially to the value of the volume, and give one a splendid idea of the actual tints of the skin observed in the various diseases.

The description of the various diseases is preceded by an interesting historical sketch of the exanthemata, and it is worthy of note that the most dreaded of them still—small-pox was the first of which we have definite records.

The section on Variola is very full and the description with the plates should practically enable one who has never seen small-pox to recognize the disease. The section on Scarlatina written by Dr. E. P. Carter is in many respects the best in the book.

The volume fills a needed want and every student and practitioner will find it a useful book for purposes of reference.

Dorland's American Illustrated Dictionary. The American Illustrated Medical Dictionary. For Practitioners and Students. A Complete Dictionary of the Terms used in Medicine, Surgery, Dentistry, Pharmacy, Chemistry, and the kindred branches, including much collateral information of an encyclopedic character, together with new and elaborate tables of Arteries, Muscles, Nerves, Veins, etc.; of Bacteria, Micrococci, Streptococci; Eponymic Tables of Diseases, Operations, Signs and Symptoms, Stains, Tests, Methods of Treatment, etc., etc. By W. A. NEWMAN DORLAND, A.M., M.D., editor of the "American Pocket Medical Dictionary." Second edition, revised. Large octavo, nearly 800 pages, bound in full flexible leather. (Philadelphia and London: W. B. Saunders & Company, 1901.) Price, \$4.50 net.

A notice of this convenient book of reference appeared in a recent number of the BULLETIN. There is little to be added in regard to the present edition as the changes which have been made are simply those which did not involve any disturbance of the pagination of the first edition. About one hundred new terms and definitions have been added without the sacrifice of any important words, in the former edition. To those physicians who desire a handy volume to lie upon the desk for ready consultation, this book may be commended as probably the most handy one in print. It is to be regretted that works of reference of this character which in the growing state of medical science are subject to constant change, are not printed by the linotype process, so that changes and additions can be freely incorporated in every edition. When the

books are printed from stereotype plates, the necessity of fitting the new word into a specified pre-arranged space often renders the definitions unsatisfactory and the information which is given of a meagre ten-word-telegram character. This edition is clearly printed on thin paper and attractively bound in flexible leather.

Diseases of the Intestines. Their Special Pathology, Diagnosis and Treatment, with Sections on Anatomy and Physiology, Microscopic and Chemie Examination of the Intestinal Contents, Secretions, Feces, Urine, Intestinal Bacteria and Parasites; Surgery of the Intestines; Dietetics; Diseases of the Rectum. By JOHN C. HEMMETER, M.D., Philos.D., Professor in the Medical Department of the University of Maryland. In two volumes. Vol. I. Octavo: 742 pages. (Philadelphia: P. Blakiston's Son & Co., 1012 Walnut Street, 1901.)

In first taking up this volume one is at once impressed with the apparent magnitude of the work. When realizing, however, that it is only the first of two volumes, the second to appear later, one is almost overwhelmed. The work cannot be considered a students' text-book, for, with the demands now made on medical students, there is rather too much chaff to be searched in order to get at the wheat. We observe a verbosity of style which has not been absent from the author's previous publications. In justice to the author, however, the treatise is rather intended for the practitioner, for he says, "My own efforts, in this present publication, have been directed to furnishing the practitioner with a complete work, from which he may readily instruct himself concerning the most approved and modern methods of diagnosis and treatment of intestinal diseases."

The present volume is largely the work of the author, although it is in part a collaboration. The section on the "Anatomy and Histology of the Intestines" is written by J. Holmes Smith, M.D., of the University of Maryland; that on "Intestinal Bacteria" by Wm. Royal Stokes, M.D., and that on "The examination of the Feces and Urine" by Harry Adler, M.D., both of the same institution. The Section on "Diseases of the Rectum" is by Thomas Charles Martin, M.D., of the Cleveland College of Physicians and Surgeons. The scope of the present volume is given in the title above. We prefer to reserve a fuller review and criticism of the work until after the appearance of the second volume, when fuller justice to the author can be done. The publishers have produced a most creditable volume. The paper and type are unusually good and the numerous reproductions excellent.

A Manual of the Practice of Medicine. By GEORGE ROE LOCKWOOD, M.D., New York. (Philadelphia and London: W. B. Saunders & Co., 1901.)

This work is smaller in size than the average text-book of medicine. The author in his preface says, "It is hoped that the work will meet the requirements of those who heretofore have been obliged to resort to the larger works of reference with which medical literature is so well supplied." This does not give a very clear idea as to the purpose of the book unless it be meant to take the place of the usual text-books. As we have said before, there should be no place for works designed to replace the standard text-books of medicine. It is probably possible to put the essential points of a text-book article in smaller space but any gain from doing so is doubtful. The authors of standard text-books, in all probability have already put the matter in as small a space as is consistent with their highest utility. Dr. Lockwood has in this work generally used his pages to good advantage but we may be pardoned for

doubting the necessity of his doing it at all. There are some points in the article on typhoid fever to which attention might be drawn, as an example of the evil of too much condensation. There is no mention of the frequent occurrence of typhoid bacilli in the urine apart from abscess of the kidney or pyelitis. In discussing relapses it is said that the interval between the original attack and the relapse "may extend to twenty-five days." This conveys the impression that this interval is the maximum, whereas it may be much longer. Then to say that "leucocytosis in typhoid fever is not marked" hardly gives a correct idea as to the usual diminished number of leucocytes in ordinary cases. Under the head of treatment, among other foods which *are to be avoided if possible* is included white of egg with water. If there is one form of diet which is useful above all others in typhoid fever, it is egg-albumen. We are quite in accord with the advice to avoid beef-peptonoids and beef-tea. That the main object of the Brand treatment is to reduce the fever, as is rather suggested, will hardly be supported by those who use it most. Its influence on other symptoms is of certainly equal importance. We would also take issue with the author in regard to his treatment of perforation, namely, "by warmth to the body and free stimulation, while opium should be given in full doses." In a robust person or during convalescence it is advised that operation "should be considered." Surely he who so advises has read but indistinctly the recent results of operation even in the most desperate cases. There is only one treatment for perforation and that is surgical, unless of course the patient be moribund when the diagnosis is made.

It must not be supposed that we take issue with the author as frequently in every article as in the one on typhoid fever, but we have given enough to show why we can not recommend his book without reserve.

Mt. Sinai Hospital Reports. Volume II, for 1899 and 1900. Edited for the Medical Board. By PAUL F. MUNDE, M.D., 1901.

This is a volume of 540 pages which contains the statistical reports of the various services and notes of many of the more interesting cases. The statistics are conveniently tabulated for reference. Among the medical reports is the account of an interesting series of six cases of diphtheria coexisting with typhoid fever, contributed by Dr. Manges. There are two articles by Drs. Bull and Libman on a case of Systemic Pyocyaneus Infection and on Interstitial Nephritis and Arteritis in the young. The surgical reports give the clinical notes of many cases and statistics of the results with added explanations as to the general rules of treatment and methods of operation. A valuable feature is the report of the anaesthetics. We notice that there is a marked preference for the use of chloroform. Several papers on various subjects in gynaecology, eye and ear work, etc., conclude the book.

An introduction to Physiology. By WILLIAM TOWNSEND PORTER, M.D., Assoc. Prof. of Physiology in the Harvard Med. School. (Cambridge: The University Press, 1901.)

This book differs from most laboratory manuals in that the description of apparatus and methods of experimenting is accompanied by a certain amount of text in which the theoretical side of the experiments is dwelt upon to some extent. It seems therefore to be more complete than the usual laboratory books, for the ground that it covers, and is particularly well adapted to the use of earnest students capable of self-instruction. The preparation of the book shows great care, and the various forms of simple apparatus that have been designed to take the place of the more complicated instruments known to

the laboratory workers, are worthy of especial commendation for their simplicity and economy. Indeed there can be no doubt that Dr. Porter's efforts to create an outfit of inexpensive apparatus suitable for laboratory experiments, will prove ultimately of great benefit to the teaching of physiology in the colleges and medical schools of this country. In the larger institutions under the guidance of professional physiologists and with workshops of their own, it will doubtless always remain true that each teacher will prefer his own designs for the simple apparatus used in class work, but in the majority of medical schools and in many colleges, the teachers are not likely to have the proper facilities for the construction of such instruments, and the opportunity to purchase an outfit at a reasonable cost ought to remove all obstacles to the introduction of laboratory courses.

From the standpoint of general usefulness the book suffers from a defect that is inherent to a greater or less extent in all laboratory manuals, that is, it is planned especially for the author's own courses and will therefore be difficult to use as a students' guide in the courses of other teachers, unless, indeed, these latter are changed to conform to the plan followed in the book. On the other hand, as a teacher's manual or as an aid to the individual worker deprived of the assistance of a competent instructor, the book should be most helpful, as it contains many suggestive experimental methods capable of further amplification if the necessity arises.

So far as the book purports to give an outline of the ideal course for medical students, it is in the opinion of the reviewer, open to the serious objection of lacking in simplicity. Much is touched upon, for instance in the electrical phenomena of muscle and nerve, that cannot at present be accepted as fundamental and probably therefore will have no immediate nor ultimate value to the medical student, in fact, will be more likely to lead to mental confusion than to mental enlightenment. Exactness in method and in reasoning can be secured best by experiments where results are clear and where meaning can be interpreted with reasonable certainty. So far as medical students are concerned, experimental work in Physiology should be planned with some reference to its usefulness in their future work. To reach this desirable end no sacrifice need be made in accuracy or training, it is only necessary to exercise care in the selection of the subjects and methods employed.

W. H. H.

A Text-Book of Medicine for Students and Practitioners. By Dr. ADOLF STRÖMPFEL, Professor and Director of the Medical Clinic at the University of Erlangen. Third American edition, translated by permission from the Thirteenth German Edition, by HERMAN F. VICKERY, A.B., M.D., and PHILIP COMBS KRAEP, A.M., M.D., with Editorial Notes by FREDERICK C. SHATTUCK, A.M., M.D. Octavo, 1242 pages, with one hundred and eighty-five illustrations in the text, and one plate. (New York: D. Appleton & Company, 1901.)

This admirable text-book continues to retain its deserving popularity. For the student and active practitioner it is an excellent work. It contains probably more reading matter than any other one-volume text-book on medicine published in English. The pages are larger and the type rather smaller than in most medical books. The illustrations have always been a feature of this work and they undoubtedly enhance its value. No text-book is so good, however, as to be beyond criticism. Were it not for the fact that the translators and editor have made many valuable additions and comments, the room for criticism would have been even greater. It is really rather surprising that a number of important observations of comparatively recent date have escaped the author's attention, a few of which are also omitted by the translators.

In reviewing the book, the section on diseases of the nervous system is, as it always has been, undoubtedly the best. We know of no text-book in which this department of medical diseases is better treated. The chapters on cardiac, constitutional and renal diseases are excellent.

In the chapter on typhoid fever we fail to find any mention whatever of typhoid cholecystitis, a not unimportant complication of the disease. We fear that the author has not fully appreciated the beneficial results from early surgical interference of typhoid perforation. He says, "If perforation occurs the treatment is much the same (as in haemorrhage). Above all, opium must be used in still larger dose, but, unfortunately, as a rule, in vain. The surgical treatment of peritonitis has rather more of a future and more success, but experience of this is still scanty." The statement is far too conservative when one remembers that in the hands of some surgeons there have been recoveries in from 30 to 45 per cent of the cases operated on, while at the most without operation only 1 or 2 per cent recover. The chapter on dysentery seems decidedly incomplete without any reference to Shiga's bacillus (bacillus dysenteriae), especially as this organism is now regarded as almost a specific germ in one form of this disease. The translators have saved the article on malaria by a very brief reference to the relation of the mosquito to the transmission of the disease. It seems strange that plague should have been omitted in the German edition. The chapter on this disease has been added by one of the translators. The Germans have been extraordinarily slow in recognizing the importance of an eosinophilia in trichinosis, from a diagnostic standpoint. No mention of this association was made by the author, although there is a brief reference to it in the translation. The old terms typhlitis and perityphlitis are retained. No reference is made to the theory

as to the etiology of scurvy which is now finding many adherents, namely, that the disease is due to toxic materials in the foods—some unknown organic poison the product of decomposition, and not to an absence of fresh vegetables or the salts of fruits and vegetable. The chapter on diabetes mellitus is very good. No reference is made to the hyaline degeneration of the islands of Langerhans found by Opie in the pancreas in a considerable number of cases of diabetes, an observation which seems destined to be of great importance in the pathology of diabetes. These are some of the sins of omission that have occurred to us. We make no hesitation in stating, however, that in our judgment the book has few equals and we doubt whether it has a superior in any language.

A Syllabus of New Remedies and Therapeutic Measures, with Chemistry, Physical Appearance and Therapeutic Application, United States Pharmacopeial Convention, 1900; American Medical Association; New York State Medical Association, United States Pharmacopeial Convention, 1900; American Chemical Society, p. 229. Price \$1.00 net. (Chicago: G. P. Engelhard & Co., 1901.)

The purpose of this book, as stated in the preface, is to furnish the busy practitioner with an accurate, condensed review of the reports on the new remedies, especially on those which synthetic chemistry has added to the physician's armamentarium. The matter, however, has been too much condensed to make the book of very much value to any one wishing to make a serious, thorough trial of any of the drugs mentioned, but as a means of quickly ascertaining something of the nature and application of these remedies, the work is of some value to the student.

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## THE TREATMENT OF VESICO-VAGINAL AND RECTO-VAGINAL FISTULÆ HIGH UP IN THE VAGINA.

BY HOWARD A. KELLY, M. D.

It sometimes happens that, in the course of a vaginal hysterectomy for carcinoma of the cervix, or for uterine fibroids, the bladder is wounded either by intention or by accident, and a vesico-vaginal fistula results which it is often difficult to close.

The chief source of difficulty in handling such a fistula lies in its distance from the exterior, on account of which denudation and suturing are awkward; additional trouble is also caused by the proximity of scar tissue in the vaginal vault, which renders the tissues less plastic and less ready to heal when approximated.

I wish to urge a method of treatment of such fistulæ which I believe to be best adapted to overcome the difficulties. It consists in opening the peritoneal cavity widely from side to side, so as to free the bladder from its fixation at the vaginal vault and render it thoroughly mobile. By this means it becomes possible to displace the entire affected area downward to any extent required, and as that part of the bladder which lies above the vaginal vault, contiguous to the fistula is thus exposed, the latter can be included in the area of denudation, if necessary.

Before beginning the operation, the patient is placed in the knee-chest position, when the bladder becomes spontaneously distended with the air that rushes in through the fistulous orifice. This posture I now use in almost all vesical operations for the following reasons: The distended bladder

can be easily and quickly incised in the vesico-vaginal septum, and then examined most satisfactorily by the finger, by the mirror, or by direct inspection. During any such operation the blood runs down the capacious vesical reservoir formed by the vertex, doing away with the necessity for constant irrigation or sponging. The actual amount of bleeding is far less than under other conditions. The field of operation is conveniently placed so that the operator works on a plane below or in front of him, and not above him. The tissues being tense are more easily handled than tissues that are flaccid and collapsing. Lastly, a great advantage is found in the fact that when vesical and vaginal tissues stretched in this way are incised, they tend to slide apart in different planes, so that it is easier to lay bare adjacent portions of the bladder in detaching the vagina.

The steps in the operation are as follows:

(1) The patient having been placed in the knee-chest position, her body is properly supported, and her neck well protected from pressure by soft cushions.

(2) The vagina is thoroughly cleansed for the operation. This may be done before taking the position.

(3) The vault is opened in the line of the transverse scar through into the peritoneum, by making a small incision in the attenuated septum. As soon as this is done the air rushes in and the viscera drop towards the diaphragm.

(4) The little opening is now extended as widely as pos-

sible from side to side, destroying the vaginal vault and setting the bladder free.

(5) A large gauze pad with a stout thread attached is next thrust down into the peritoneum, and by pulling on this the bladder is crowded towards the vaginal outlet while the peritoneal cavity above is protected. It is important throughout to wipe out the cavity of the bladder from time to time in order to avoid the escape of any of its contents onto the peritoneum.

(6) The margins of the fistula are now split, separating the vagina from the bladder, or if the operator prefers the older methods, the fistula is denuded on all sides.

To split the margins I use a short-bladed, thick knife, sharpened on both edges and set in the handle at an angle of about 45 degrees as shown in the figure; this is better than a longer thinner blade, which tends to perforate the flaps. See Fig. 1. An ordinary scalpel or a bistouri cannot be used.

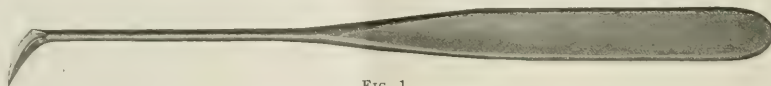


FIG. 1.

(7) When the edges are split and the bladder wall is set free, the bladder is sewed up separately by means of a row of buried sutures of fine silk or of catgut, thus uniting the muscularis alone, by this means the vesical edges are turned up into the cavity of the bladder, forming a little buttress (Sänger and others).

The vaginal surface is then united with a row of fine silkworm gut sutures. I use by preference a grade of gut which is reckoned inferior in quality, because it is finer and more flexible. This row of sutures may be continued up onto the peritoneal surface of the bladder, in this way easily and securely covering in that upper part of the fistula which under previous methods of treatment was least likely to heal. There must be no dead space left between this and the buried row of sutures. The silkworm sutures are cut off at about 4 cm. from the knot.

(8) The fistula being now closed, the pack is withdrawn, and then in order to get rid of the air in the peritoneum, the cavity is filled through a tube with a normal saline solution which, as it rises to the level of the vagina, displaces the air. When the patient is turned over onto the dorsal posture all the water escapes.

(9) A little suturing at each angle and a drain of washed-out iodoform gauze (Sänger) in the middle, and one in the vagina complete the operation and the dressing. It is best to keep a catheter in the urethra for from 7 to 9 days following the operation. I have closed several fistulae of this group by opening the peritoneum, but I have not as yet made the wide lateral dissection proposed here.

An accident revealed to me another plan of treating fistulae which may sometimes prove a valuable resource.

I cured the fistula in question by first making it larger and thus securing the coaptation of the more difficult and inaccessible part; and at a subsequent operation I closed

the newer portion which was easy of access. The method in detail was as follows:

The patient (San. No. 9237) had a vesico-vaginal fistula about 1.5 cm. in diameter, situated at the vaginal vault in the midst of an area of unyielding scar tissue, following a vaginal hysterectomy for carcinoma. She had had eleven unsuccessful operations before I saw her. I attempted at the twelfth operation, the patient was in the knee-chest posture and with the perineum elevated by a speculum, to free the fistula and make it easier to handle by first incising the thin septum at the vault and opening the peritoneum for 2 or 3 cm. from side to side, but I did not make the broader lateral incisions recommended above. The next step in the operation was to cut through the vesico-vaginal septum from the lower margin of the fistula down into the vesical trigonum. This enabled me to separate the bladder from the vagina with ease all around the edges of the fistula, which were not pared at all, and no tissue whatever was

removed. The vesical walls were then turned in towards the bladder cavity and the muscularis vesicae united by fine interrupted catgut sutures. The vaginal walls were then closed with similar catgut sutures over the line of union of the bladder. The lower part of the wound nearer the urethra was approximated also with catgut.

Union failed in this lower tract where the new wound was made and succeeded in the upper more rigid and more inaccessible portion.

A second operation was then done by simply paring and uniting the edges of the fistula with interrupted silkworm-gut sutures, including all the tissues up to the vesical mucosa.

This operation succeeded perfectly and the patient returned to her home in Michigan completely restored.

The plan of separating the bladder on all sides from its peritoneal attachments in order to mobilize it, and make it more accessible to surgical treatment, can also be applied with even greater satisfaction to recto-vaginal fistulae situated high up in the vagina. In this case the absence of the uterus is not needed to facilitate the exposure of the fistula, as it is only necessary to open the peritoneal cul-de-sac behind the cervix widely from side to side and down at the sides of the rectum to gain the great advantage of increased mobility of the bowel, including an area above the fistula which can also be turned in by sutures so as to cover in the upper angle of the opening.

I prefer in these cases, after completely detaching the vagina from the bowel, to infold and sew up the bowel separately with fine silk sutures in one or two layers, and then I do not attempt to close the vaginal wound over the bowel, but put a little iodoform gauze drain between the edges of the vaginal opening and allow the wound to close by granulation. An opening should be left in the peritoneum wide enough to admit a small iodoform gauze drain.

CYCLIC ALBUMINURIA.<sup>1</sup>

BY WM. E. HUGER, M. D., Charleston, S. C.,

*Formerly Clinical Assistant in Genito-Urinary Surgery, The Johns Hopkins Hospital Dispensary.*

Two years ago, two very interesting cases of albuminuria came under my observation, and it has been my good fortune since to be able to follow them closely. Case I came to the Genito-Urinary Department of the Johns Hopkins Hospital with an acute attack of gonorrhoeal urethritis, and it was only after this had subsided somewhat that the disease with which my paper deals was discovered. Case II was first seen by Dr. Thomas in the Neurological Department of the Hospital, and was subsequently turned over to me, because of my interest in his accidentally discovered albuminuric condition.

## HISTORIES.

CASE I.—W. W., age 18 years. Sept. 6, 1899.

*Complaint.*—Urethral discharge.*Family History.*—Negative.

*Past History.*—Only measles of the children's diseases. Always a fairly strong boy. Never any pain in the abdomen. No colic of any kind. No previous attack of gonorrhoea. No syphilis. At the age of twelve he began to masturbate and has continued about two or three times a week since then. About one month ago began going with women. Has never had his urine examined.

*Present Illness.*—A running from urethra began four days ago. Incubation four days. All the symptoms of a mild gonorrhoea were present, but no complications. Works in a barber shop and takes very little outdoor exercise.

*Physical Examination.*—Rather an anæmic boy but fairly well developed. Heart, an extremely faint systolic murmur at apex in the 5th interspace just outside the nipple line. Second aortic not accentuated. Arteries soft. Tension low. Lungs negative. Abdomen soft, no tenderness. Kidneys not palpable. Genitalia small but normal. Slight purulent discharge from the urethra. Microscope shows it to contain leucocytes and epithelial cells, intra- and extra-cellular, biscuit-shaped diplococci decolorizing by the Gram stain. Urine: 1st glass very cloudy with pus; 2d glass clear with no shreds.

The patient paid three visits a week for about one month and had the varying ups and downs to which many gonorrhoeal cases are subjected. At the end of this time the urine having cleared up sufficiently, I tested for renal albumin and was surprised to find an abundant precipitate on boiling the urine, which did not clear up on the addition of acetic acid. The test was repeated with a carefully filtered specimen and the same result obtained. Hyaline casts were found in great numbers in a centrifugized specimen, the urine having been voided at 12.30 p. m. The next day an examination made at 9.30 a. m. showed less albumin

and fewer casts. A third specimen voided on rising and brought to me showed no albumin and no casts.

He was then sent into one of the medical wards at the hospital, where he remained three days. He was put to bed, and placed on a milk diet for two days, but as the report of "no casts and no albumin" was made, on the third day he was allowed to get up and was put on a meat diet. His urine examined on the fourth morning being again negative, he was sent home. I wish here to call attention to the fact that the urine examined in the hospital was in each case that passed in the morning after prolonged rest in bed. As I proved later, had the urine been voided and examined at intervals during the day, the observation would have been different.

On the morning after leaving the hospital the patient came to the dispensary again, and as before, the urine passed contained a quantity of albumin (.2 per cent) and a number of casts, hyaline, granular and a few epithelial.

The patient was given eight two-ounce bottles which were to be used as follows: He was to urinate in the first one just before retiring; in the second, about an hour later; in the third, on rising; in the fourth, one hour after breakfast; in the fifth, at 12 m. (just before dinner); in the sixth, one hour after dinner; in the seventh, at five o'clock (just before supper); and in the eighth, one hour later. The object of urination at bedtime and a half-hour later was to wash out any albuminous urine which had descended from the kidneys previous to lying down, in order that the morning specimen might be urine secreted only while the body was in the horizontal position.

CASE II.—H. C., age 18 years; drug clerk. Dec. 10, 1899.

*Complaint.*—Nervousness and eye trouble.

*Past History.*—No malarial fever, no scarlet fever, no diphtheria. Has had measles and whooping-cough. No venereal disease. Four years ago patient had a severe fright, his life being threatened by some man. Has masturbated quite frequently but has never had sexual connection. Three years ago his mother died and he had a slight hysterical attack. Then, none again until the present time.

*Present Illness.*—Three weeks ago the patient had a return of the "fits" like the one which occurred when his mother died. This time they were frequent and accompanied by a severe pain in the left frontal and temporal regions. The pain has been present during the entire time, but is most intense just before and after a "fit." He was obliged to go to bed and has only just left it for the purpose of consultation. The bowels are regular, and except for a marked nervousness there is nothing unusual in his history.

*Physical Examination.*—Slender, nervous looking youth, apparently backward for his years, both mentally and physio-

<sup>1</sup> Read before The Johns Hopkins Hospital Medical Society, June, 1901.

ally. Occasional twitching of both eyelids and of the muscles of the mouth. Eyes: right one normal; left has a distinct optic neuritis (Dr. Reuling); measurements not made. Lungs negative. Heart negative. Arteries soft, pulse of high tension. Abdomen negative. Kidneys not palpable. Penis and testicles normal. Urine varies as will be described.

This case was followed in exactly the same manner as the

Both were young men, one healthy and uncomplaining (except for gonorrhoea), the other nervous and sickly. Both had been in the habit of masturbating, but probably not more than the average boy. Neither showed any albumin in the urine voided on rising. Both reached their maximum amount (.2 per cent) about four or five hours after rising, and had a gradual decline in the next six or seven hours,

1899.	P. M. 8.30	P. M. 9.30	A. M. 6.30	A. M. 8.30	A. M. 10.15	M. 12	P. M. 12.15	P. M. 1.30	P. M. 5	P. M. 6.30		Remarks.	
Nov. 8.	1011	1007	1015	1015	1016	1020	..	1020	1012	1013	Sp. gr.	The amount of albumin was rarely ever the same at the same time each day.	
Nov. 9.		Trace	None	Much	Much	Quant'y	..	Quant'y	Some	Some	Albumin		
Nov. 10.	Few	Few	None	Many	Many	Many	..	Many	Few	Few	Casts { hyaline granular epithelial		
Nov. 13.	1015	1005	1015	1022	1020	1019	..	1015	1015	1012	Sp. gr.	The evening of the 13th the albumin and casts were greatest without apparent reason.	
Nov. 14.	Much	Less	None	Much	Quant'y	Quant'y	..	Quant'y	Much	Less	Albumin		
Nov. 15.	Some	Few	None	Some	Many	Many	..	Many	Some	Fewer	Casts { hyaline granular		
Nov. 19.	1023	1006	1020	1015	1020	1020	..	1012	1020	1022	Sp. gr.	In spite of severe exercise, no increased albumin was found on the evening of the 19th.	
Nov. 20.	Trace	None	None	Trace	Slight	Quant'y	..	Much	Much	Much	Albumin		
Nov. 21.	One	None	None	Some	Few	Many	..	Some	Some	Some	Casts { hyaline granular		
Nov. 26.	1015	1004	1014	1007	1011	1012	..	1016	1015	1010	Sp. gr.	Patient voided on first coming in and then sat quiet until 1.30 P. M., yet this second spec. showed more albumin.	
Nov. 27.	Trace	None	None	Trace	Some	Gr. quant'y	..	Much	Much	Less	Albumin		
Nov. 28.	Two	None	None	Few	Some	Many	..	Some	Some	Fewer	Casts—hyaline		
Dec. 1.	Spec. I				1015	Some	Spec. II	1015	..	..	Sp. gr.	Voided at 12 M., then put in horizontal position. Voided at 12.15 P. M., keeping same position, and, rising at 1.30 P. M., voided again.	
Dec. 3.	Spec. I				1016	Some	None	1012	..	..	Albumin		
Dec. 4.	Spec. I				1016	Some	None	1012	..	..	Casts { hyaline granular epithelial		
Dec. 5.	1024	1020	1023	1018	1019	1015	..	1015	1017	1020	Sp. gr.	Patient went to bed at 11 A. M., ate a regular meat and vegetable dinner in bed.	
Dec. 6.	Trace	Trace	None	Some	Some	Much	..	Much	Some	Trace	Albumin		
Dec. 7.	Two	Few	None	Few	Some	Many	..	Many	Few	Fewer	Casts		
Dec. 8.	1006	1005	1011	1006	1010	1012	..	1015	1007	1008	Sp. gr.	Patient went to bed at 11 A. M., exercised vigorously sitting up in bed. At first exam., 10.15 A. M., he had not yet exercised.	
Dec. 9.	Some	Trace	None	Some	Some	Quant'y	..	Gr. quan.	Some	Some	Albumin		
Dec. 10.	Few	None	None	Some	Some	Many	..	Quant'y	Few	Few	Casts		
Dec. 11.	Each of these was a twenty-four hour specimen				1010	1007	1015	1011	1012	1012	Sp. gr.	Patient voided at 10.10 A. M., was then laid on a table. In 25 minutes he voided again (10.35 A. M.). At 11.10 he was gently raised into the erect position and in 20 minutes voided again.	
Dec. 12.	Each of these was a twenty-four hour specimen				Some	Some	Some	Slight	Some	Much	Albumin		
Dec. 13.	Each of these was a twenty-four hour specimen				Few	Few	Some	Few	Few	Many	Casts		
Dec. 14.	Each of these was a twenty-four hour specimen				..	..	..	..	..	..	..		
Dec. 15.	Each of these was a twenty-four hour specimen				..	..	..	..	..	..	..		
Dec. 16.	Each of these was a twenty-four hour specimen				..	..	..	..	..	..	..		
1900.													
Feb. 18.	1017	1010	1020	1015	1015	1023	..	1020	1009	1015	Sp. gr.	Patient went to bed at 11 A. M., ate a regular meat and vegetable dinner in bed.	
Feb. 19.	Some	Trace	None	Some	More	None	..	None	Some	Some	Albumin		
Feb. 20.	Some	None	None	Some	More	None	..	None	Some	Some	Casts		
..	1015	1008	1023	1014	1010	1006	..	1011	1020	1020	Sp. gr.	Patient went to bed at 11 A. M., exercised vigorously sitting up in bed. At first exam., 10.15 A. M., he had not yet exercised.	
..	Trace	Trace	None	Some	Some	Much	..	Much	Some	Less	Albumin		
..	Few	Two	None	Some	More	Many	..	Many	Some	Fewer	Casts		
..	..	..	..	..	A. M. 10.10	A. M. 10.35	A. M. 11.30	Patient voided at 10.10 A. M., was then laid on a table. In 25 minutes he voided again (10.35 A. M.). At 11.10 he was gently raised into the erect position and in 20 minutes voided again.					
..	..	..	..	..	Much	None	Much						
..	..	..	..	..	Many	None	Many						

Three dates are grouped because the 8.30 P. M., etc. hours are on date Nov. 8th, for instance, the 6.30 A. M. the next morning, Nov. 9th, and the 10.15 A. M. specimen, and occasionally others about that time, was voided the day following, Nov. 10th in my presence, when the patient brought me the bottles of his urine passed on the two days previous, as directed.

other, but owing to the hysterical attacks, I was obliged to keep the patient in bed for a period of three weeks, which fact gave added data. Both of these cases were so very similar in their course under the same conditions that, although they were examined equally carefully, I will only give a detailed description of the different specimens of urine belonging to Case I, a simple analysis of the urine of Case II, and then note where differences occur.

but no absolute disappearance of the albumin until the body was again in the horizontal position. Case I has continued in much the same condition as when first seen (Sept. 6, 1899-Sept. 1, 1901). Case II was first seen Dec. 10, 1899, and ran his usual course until Feb. 22, 1900, on which date I made the following note:

"This afternoon the patient was seen at his home and in bed. For several days he has been having two and three

convulsions daily. While sitting by his bed, suddenly he told me that a 'spell' was coming on and that he was powerless to prevent it. The eyelids began to twitch, then the lips, fingers and arms. The motions increased in rapidity, becoming very rapid. Suddenly, with a quick movement the right or left hand would be grabbed between his teeth and held firmly in spite of vigorous efforts made by me to release it. The eyes assumed a wild vacant stare. At times he snarled like a dog. Finally, the head fell back and the patient was in a position of mild opisthotonos. The attack lasted ten minutes and then consciousness which had been lost from the beginning was gradually regained. For sometime, about half an hour after he regained consciousness, he was unable to see out of the left eye (the one in which the optic neuritis was found). The urine passed just after the attack was clear, acid, sp. gr. 1026, no albumin, no casts and no sugar."

For three weeks he was confined to his bed, having these hysterical attacks in gradually decreasing numbers and intensity. Never once during this time did any albumin appear, and for three months afterward it was absent, although the patient was up and about as usual. At the end of that time there was a recurrence of the albumin as before, only the maximum amount was increased to .25 per cent. He has had but one slight hysterical attack since those above described.

I will add a few remarks in explanation of the urine chart. As I have said before, the chart belongs, strictly speaking, to Case I, but Case II differed in no material way from it.

The hour 8.30 p. m. is taken as the starting point, because then it was that the patient voided into his first bottle and next at 9.30 p. m., so as to prepare his bladder for the reception of the urine secreted during the night. It is understood also that the patients went to bed at 8.30 p. m. and did not rise again, except at 9.30 p. m. to void, until 6.30 a. m., when the third specimen was obtained. This last was the urine secreted with the body in the horizontal position. Under "remarks" on the urine chart will be found notes on special experiments.

Once every month up to Sept. 1, 1901, I have examined the eight specimens of urine, the patient continuing his daily life. Each time the result has been as detailed above. On Jan. 7, 1901, I examined a specimen from Case I, voided at midnight after the patient had been on his feet working from the early afternoon until that hour. There was only a trace of albumin and one or two hyaline casts. Distinctly less than was usually found in the 8.30 p. m. specimen.

The cases of cyclic albuminuria detailed above differ from almost all others reported in that they both show casts in abundance. I found a few previous records in which casts were mentioned either as a possibility in these cases or were mentioned as being found now and then in the specific reports, but nowhere were the casts said to be present, as in these cases, whenever albumin was found and in proportion to the amount. The casts were principally hyaline of

the small variety, but often the granular variety was present, and on several occasions definite *epithelial* casts were found.

To determine approximately the relative number of casts, I took fifteen cubic centimeters of urine from each specimen and centrifugalized this quantity for five minutes at between 1200 and 1500 revolutions per minute, then examined under the microscope for fifteen minutes when the casts were very few or none at all. When they were numerous, prolonged search was of course unnecessary. The amount of albumin reached .2 per cent about midday, though it was not so high every day. The chemical character of the albumin (serum-albumin) will be spoken of later.

In neither case did food have any influence on the amount of albumin eliminated. A relatively larger amount of albumin was just as apt to be in the urine passed just before dinner (12 m.) as in that passed an hour after. At no time was either the merest trace of albumin or any casts found in the early morning specimen, and only once in any great quantity during the evening. For this last I can assign no reason. Once at 9 p. m. I made the patient run for a half-mile before voiding, but the quantity of albumin was not increased above the amount usually found at that hour.

On several occasions the patients went to bed at eleven o'clock in the morning, voiding on lying down and again soon after. Both these specimens contained albumin and casts in the usual amounts. Dinner was eaten in the reclining position, and then the urine voided on rising an hour and a half later contained neither albumin nor casts. But the five o'clock specimens had their customary albumin and casts.

The urine passed thirty-five minutes after lying down showed no albumin and no casts, provided the bladder had been emptied soon after reclining for the reason before stated. But in twenty minutes after the erect position had been assumed, no matter if the patient had been gently and slowly lifted into it, albumin and casts reappeared. The quantity of albumin after a change of this kind was always even greater than before lying down, but soon returned to the same amount and then continued to increase or decrease according as it had been previously on the increase or decrease. The relative position of the legs and body if the patient sat in a chair made no difference, a small amount of albumin and corresponding number of casts being secreted. Only on rare occasions did I find oxalate crystals.

The amount of literature on the subject of cyclic albuminuria, as may well be imagined, is extensive because beside the scientific interest in the disease, it bears a very close relation to the business risks involved in life insurance. Many writers have watched their cases pass through the cyclic stage to a successful recovery, one or two have seen Bright's disease develop, and again a great number have noted that the cyclic symptoms were still manifest at the time of their publications. These last should interest us most because the first two are settled and we need the other to help decide beyond a doubt the uncertain question of prognosis. Unfortunately, there seems very little chance

that many will continue their reports, or that others will take up at a later date, those cases already reported.

No post-mortem has been performed on a case known to have been suffering from cyclic albuminuria at the time of death, so that the pathological condition is based on theory and differs as widely as conclusions so supported always do.

Up to the year 1878, any albumin in the urine was generally considered as indicative of a very serious result and little hope of recovery was expressed. At this time Moxon (1) published a paper in which he speaks of Intermittent Albuminuria, or the albuminuria of adolescence and of Remittent Albuminuria. He reports seven cases of the former, but refers only in a general way to nineteen coming under the head of Remittent Albuminuria. He says that in these latter the albumin is present in greater or less quantity during the day, especially in the urine passed after breakfast, but that no albumin is present in the urine passed on rising from bed after a night's rest. He divides them into two groups: (a) In which there is no reason other than the albumin to suspect the existence of renal disease, and (b) where further symptoms show that the renal system is seriously at fault, in fact, that Bright's disease exists. He says that the pulse is of low tension. No cases were recorded individually. Johnson (2) had already drawn attention to the same facts in 1873. He believes that most cases of cyclic albuminuria are merely cases recovering from an acute attack and that they can always be traced to the exciting cause. Later (3), he showed that whether or not Moxon was right, he did not give sufficient data for drawing his conclusions. Rooke (4) gives two cases, ages 14 and 16 years. In one the urine was examined several hundred times and never once was albumin found in the morning specimen. The patient was kept in bed once for three weeks. During this time there was an absolute disappearance of the albumin, but immediately on rising it reappeared. In the other case the results were the same with similar experiments. In 1881, Dukes (5) mentioned an albuminuria which could be gotten rid of in an hour or two by putting the patient to bed and could be reproduced almost at will by getting him up.

World-wide interest in this peculiar condition was not aroused until Pavy (6), in 1885, described very minutely the clinical changes in what he called "Cyclic Albuminuria." He mentions six cases, all young men. Two were seen a year later, one had no albumin and one only a trace at midday. Three were seen two years later and none had albumin. The sixth was followed for four years, during which time the condition lasted. In 1886 (7), he added three more cases to the above, two boys and a girl. All his patients were free from albumin on rising, had more or less present at midday, and with some it was absent in the evening before going to bed, but most had a trace as long as they were up. The albumin was present in spite of fasting during the morning when they were not in bed, but, if they remained in bed, none appeared in spite of much food or even a cold bath. Since Pavy's time a great deal has been written, and

yet only in a few details do the accounts differ from his, hence by many it is called Pavy's disease. Probably Pavy's own term, Cyclic Albuminuria, is the best, because although it is cyclic only under the same daily conditions, those are the ones under which we live and we are obliged to change those conditions when we wish an alteration in the cycle.

One statement in his article started a discussion that has been taken up the world over and of which we have not yet heard the end. Another is of especial interest when taken in connection with this paper. First, he unhesitatingly calls the disease functional, says that there is nothing to show that it is the beginning of Bright's disease or that it leads to anything serious. Second, that no tube casts are found. This last has been accepted and confirmed by almost every one. Kraus (8), Oswald (9) and Landi (10), who are the chief ones mentioned all through literature as having found casts, barely state this fact. Hawkins (11), too, speaks of the possibility of their presence, but gives no cases. Marie (12) says that casts sometimes appear but that there were none found in the case which he reports.

*Symptoms.*—Often there is nothing to attract attention to the urine, as the patient either has no complaint or perhaps merely complains of a languid feeling and protests that he is not sick. Marie grants that symptoms are usually absent, but adds that in addition to the languid feeling there may be palpitation, neuralgia or even dizziness and epistaxis. Arnozan (13) adds neurasthenia, œdema of the face, headaches and cramps. One of my cases had absolutely no symptoms, and it was by chance alone, or rather by routine examination of all urines, that the albumin was discovered. The other case had, besides hysterical attacks, a distinct optic neuritis of one eye which improved later with an improvement in the patient's general condition. Ostwalt (14) reports two cases of cyclic albuminuria with optic neuritis and no other symptom.

#### PATHOLOGY.

Marie cannot explain the pathological condition, but believes it a functional state, certainly probable in his case. Capitan (9), de Chateaubourg (9), Leube (9), Finot (9), Zechisen (9), Lasiadke (9) and Granger Stewart (15) say that albumin is an abnormal constituent of urine, but that it can occur without any ill effects on the patient. Klugden (9), Senator (9) and Posner (9) believe albumin can occur physiologically. Pavy, as I have noted, calls cyclic albuminuria functional. Klemperer (16) says: "Every sign of Bright's disease is absent. It does not run into renal disease." Lecorché and Talamon (9), replying to Senator, are strongly in favor of the latent nephritis theory. Talamon says that some authors call cyclic albuminuria functional because they are unable to conciliate the cyclic symptoms with an organic lesion. Osler (17) maintains that the presence of albumin in the urine in any form and under any circumstances may be regarded as indicative of change in the renal or glomerular epithelium. Arnozan, too, says that albumin in urine is always pathological, that it does not

result from high tension, but may show a slowing and stagnation of the blood current, and that even in the cyclic cases it is dependent upon epithelial changes. He adds that it is due either to infection or intoxication. Ostwalt draws the following deductions from the literature and his own cases:

(1) Alterations in the walls of the vessels certainly play an important part in the production of cyclic albuminuria.

(2) In one case (of his own) certainly the change in the walls preceded albuminuria.

(3) We may believe that this change of the vessels is in consequence of destructive tissue change.

(4) The functional insufficiency of the vessel walls allows the albumin to pass into the urine when the renal vessels are in an unfavorable hydrostatic condition.

(5) Oxalate of lime circulating in the blood may act as an irritant causing albumin."

Pavy was inclined to the theory that oxalate of lime was one of the etiological factors in bringing on albuminuria. In my cases, I rarely found these crystals, although I always looked carefully for them.

Oswald and Ott (9), Beckman (9), Bull (18) and Landi believed the condition pathological. Hawkins says that the view generally held to-day is, that the actual seat of the trouble appears to be in the vasomotor mechanism, which regulates the flow into and out of the glomeruli, and not in the kidney structure itself.

Several times a question as to the character of the albumin has arisen and each time the tests proved serum-albumin to be present. I followed the tests as laid down by West (19), and in both my cases found a large percentage of serum-albumin.

#### ETIOLOGY.

*Adolescence* is the period of life most liable to the disease, but it may occur at any age. *Sex*.—It has been found more frequently in the male than the female. The percentage is still pretty much the same as found in 1895 by Dubreuilh, males 88 per cent, females 12 per cent. *Food*.—Herringham (20) tried the effects of food in varying quantities and qualities, but found that the albumin came and went according to position, but absolutely irrespective of diet. This author had one case and his report of it is well worth considering. Neither the acidity of the urine nor the relative amounts of urea and uric acid bore any constant relation to the albuminuria. During an entire month the albumin ceased, although there was no change in the patient's way of living. No casts were found, but there were plenty of leucocytes and oxalate crystals. The only thing which in any way affected the albumin was the erect position, and he concludes that it resulted from an increased weight of blood resting on the renal veins. A weak circulation and general loss of tone, common in these cases, predispose to a condition of venous stasis. The kidney by reason of its double capillary system is more liable to stasis than other parts. The greater liability to albumin in the forenoon is due to a weaker circulation at that time. Bouchard (9) claims that the al-

bumin is due to some toxicity of the blood which is greater during the activity of the morning hours, less towards evening and least of all during the quiet of sleep. These two statements are rather opposed to each other, one says the circulation is poorer in the morning and the other that it is more active. The truth is that it depends upon the actions of the individual. A vigorous circulation can be aroused morning, noon or night by making the patient exercise. When I did this, it did not matter at what hour, the presence of the albumin depended entirely upon the position of the body. Exercising violently when standing at 1 p. m. did not increase the albumin usual at that hour, and yet exercising the upper extremity and lower extremity when the body was lying down brought no albumin. Moreover, if a toxin were the cause, as Bouchard claims, it could hardly be gotten rid of in a few minutes after reclining, and yet the albumin certainly disappeared in a very short time.

The acute, infectious diseases, especially the eruptive fevers, are said to be followed sometimes by cyclic albuminuria. Marie and Johnson emphasize it. This distinctly suggests that cyclic albuminuria is merely a phase of mild degree of that true nephritis which is so frequent a sequela of the eruptive diseases. In one of my cases the albumin was first discovered after an attack of gonorrhœa, but I have no more reason for believing it to be the cause than I have in the other case to think that his condition was due to measles or whooping-cough which he had in very early childhood. An interesting point is that on the question of blood-pressure one of my cases supports the views of the advocates of low tension, while the other, with a pulse of quite high tension, agrees with the views of those who consider it to be the cause. *Heredity*.—Gout and rheumatism are supposed etiological factors. Although Heubner (21) found several cases in the same family, Lacour (22) three in the same family, Schön (23) two, and occasionally others do the same, the evidence is too circumstantial and not sufficient to consider heredity more than a coincident.

Sir Wm. Gull (24) believed that the general nervous tone of the patients was poor and that the nerve supply to the renal vessels and parenchyma was correspondingly poor and slow to work. The increased blood-pressure upon the renal vessels caused by the erect position put more work upon the kidneys than they were able to perform, and the epithelial filter allowed some of the albuminoid material in the blood to pass through. This was gradually corrected as the sluggish nerves reacted to the stimulus, and after a time the previously increasing amount of albumin began to decrease.

*Position*.—Since attention was first drawn to this disease, no one has denied that position is the most powerful factor in influencing the albumin. In all cases, albumin disappears from the urine soon after lying down and reappears after rising, no matter how the hours are changed or how long the patients lie down. If they go to bed during the day and get up at night, albumin comes and goes correspondingly. If they eat or exercise while reclining still no albumin appears, but immediately after getting up it

shows itself and increases in amount for from four to six hours, then begins to decrease, although not entirely disappearing until the horizontal position is resumed. Herringham obtained no albumin when his patient sat upright with the legs elevated, but in both of my cases if the body was raised higher than an angle of thirty degrees from the horizontal plane, I obtained albumin without regard to the relative position of the thighs. When Pavy's cases were carefully lifted into position, no albumin appeared, but in mine it did.

#### PROGNOSIS.

In 1896, the French Congress of Medicine discussed the prognosis of albuminuria at great length. Although the discussion was not confined to the so-called physiological type, it was on this that the greatest stress was laid, because, as Tessier (9) said, the prognosis of the definite, chronic, pathological nephritis was fixed. He believes that there is a functional albuminuria and that it is no more apt to become Bright's disease than a simple bronchitis is to develop into tuberculosis. His conclusion is based on twenty-eight cases of cyclic albuminuria gathered by Merley and himself and followed by them for from nine to thirteen years. Four out of this number developed Bright's disease. The others got well or had only an occasional attack. This report of Tessier contains the greatest number of cases followed during the longest period of time. He gives a very good prognosis, but surely his own statistics reverse his opinion and were we dependent upon him alone for information we could not conscientiously give our patients the hope which further study of the literature shows justifiable. Pavy, Johnson, Senator and others have seen cases pass through the cyclic stage and go on to recovery. Tyson (25) advocates admitting these cases to life insurance.

A very frequent statement, and one that at first glance appears sound, is, that the prognosis depends upon the following:

1. Length of time the albumin lasts each day.
2. Length of time the condition has been present.
3. Amount of albumin, and
4. Whether or not casts are present.

But we must remember that in everything our prognosis depends upon both or one of two known facts: (a) The known pathological condition, or (b) the clinical life history of previous similar conditions, whether or not we can obtain the exact pathology. Here the pathology is open to discussion, we have more or less fixed ideas, but we have never been able to hold the kidney in our hands and show conclusively what is to be found. But we have the clinical life history of many previous cases of cyclic albuminuria. From 1878 to the present day, as I have said, the literature is full of them, and their careful study does not bear out the conclusions above stated. An almost unbroken rule in these cases is, that the albumin appears soon after the patient gets into the erect position, reaches the maximum from four to six hours later, and then begins to decline, but does

not absolutely disappear until the horizontal position is again assumed. This practically throws out the first condition, because the length of time is the same in all.

Tessier's cases tend to show that the second condition is not true. Irrespective of the length of time the condition was present, a few continued to have exacerbations of albuminuria, the large majority recovered and four passed into Bright's disease. Statistics in regard to the amount of albumin present in each case are not to be obtained, but the majority report between .1 and .2 per cent, yet I find nowhere that those having the larger percentage in contradistinction to those having a lesser amount, passed into a continuous albuminuria. The relation between the amount of albumin and casts has yet to be studied.

The fourth condition sounds plausible from a pathological standpoint, but as a fact, only three writers say that casts were present in their cases, and they speak neither of a fatal termination nor of the development of a continuous albuminuria. The fatal results are to be found among the cases reported by men who state very specifically that casts did not occur. But I must admit a belief that with careful centrifugalization and examination casts would have been found in many cases where they were said to have been absent.

The specimens from both my cases were examined as I have described on a previous page, and I think there is no reason to doubt that they are cases of pathological nephritis. Casts were found in abundance, and not only hyaline and granular, but also on many occasions epithelial. The patients responded to all the tests reported, and in addition, while in the sitting erect position, gave albumin and the appearance of albumin, though they had been gently and slowly lifted into the erect position.

Drugs are found not to affect the disease. Many, as well as I, have tried the effects of many drugs, but there being no change due to them, it is unnecessary to consider them further.

#### CONCLUSION.

That the cyclic albuminuria, like the recognized pathological albuminuria, is due to one or perhaps all of three causes:

1st. Inflammatory and degenerative changes in renal structure, as evidenced by the finding of casts. There is every reason to think that by careful searching casts will be found far more often than previous reports lead us to believe.

2d. Alterations in the quality of the blood which render its serum-albumin more diffusible. There is nothing to prove an inferior diffusibility in these cases, but the patients are almost always anæmic.

3d. Alterations in the degree of blood-pressure. Here due to a mechanically increased pressure on the renal veins.

Having learned that occasionally these cyclic cases pass into Bright's disease, but that by far the majority have gotten well and that many have been followed for years and then lost sight of still in their same condition, it must

be admitted that Moxon and Arnozan were right in dividing them into two groups: (a) Those few which develop a continuous albuminuria, and (b) the vast majority which get well. Continued rest in bed for a prolonged period should always be urged because at any rate it removes the exciting cause. One of my cases remained free from albumin for three months after being in bed for three weeks.

I believe that by a *very careful* examination for casts a large percentage of cases will be found to contain them, and that the serious prognosis given because of their presence will be modified.

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- (3) Johnson, George: British Med. Jour., Feb. 2, 1889.
- (4) Rooke, T. Morley: British Med. Jour., 1878, Vol. ii, p. 596.
- (5) Dukes, Clement: British Med. Jour., Nov. 12, 1881.
- (6) Pavy: Lancet, 1885, Vol. ii, p. 706.
- (7) Pavy: Lancet, 1886, Vol. i, p. 437.
- (8) Kraus: Wien. Med. Presse, 1893, Vol. xxxiv, pp. 1877, 1923, 1964 and 2006.
- (9) Oswald: Reports of French Med. Congress, 1896.

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- (16) Klemperer: Zeitschr. f. klin. Med., Bd. 2, Hft. i.
- (17) Osler: Principles and Practice of Medicine, Fourth Edition, 1901, p. 855.
- (18) Bull: Berl. klin. Wchnsch., 1886, xxiii.
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- (21) Heubner: (Schön) Jahrbuch f. kindrh., 1896, B. 41, S. 307.
- (22) Lacour: Lyon Méd., No. 25, 1897.
- (23) Schön: See above, 21.
- (24) Gull, Sir Wm.: (Moxon) Guy's Hosp. Reports, 1878.
- (25) Tyson: Assoc. of Amer. Physic., 1888.
- (26) Von Noorden: Deutsches Archiv. f. klin. Med., Leipz., 1886, xxxviii, 20.

## ON A CYST ORIGINATING FROM THE DUCTUS THYREOGLOSSUS.

BY G. CANBY ROBINSON.

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The literature on the cysts of the anterior median cervical region is as yet not extensive, and although mention is made of them in all the text-books, in treating of the surgery of the neck, the actual number of cases reported is small. It has been shown by Kostanecki and Milecki<sup>1</sup> that, according to the light thrown by His on the development of the branchial arches and clefts, congenital fistulae and cysts of the neck must almost always arise from the second cleft. One case described by Virchow originated from the first branchial cleft, but the third and fourth are almost entirely excluded. The outer openings of such fistulae may be almost anywhere, but the nature of the fistula is determined by the more constant position of the internal orifice and the course of the canal. On this basis therefore cysts lying exclusively in the median line without connection with the skin or pharynx can hardly be explained as originating from the branchial clefts.

Verneuil<sup>2</sup> described cysts in the regio-thyrohyoidea, collecting descriptions of cases from the literature and discussed the possibilities as to their origin. He found several bursæ

in the thyrohyoid region and thought that cysts might arise from them. Such cysts, however, would have an endothelial rather than an epithelial lining. He gave, too, Cruveilhier's description of the pyramidal prolongation of the thyroid toward the hyoid and concluded that the case described by Rouget which he quotes, must have arisen by a cystic dilatation of some part of this prolongation. This cyst lay in the position of the thyroid pyramid, was very easily enucleated and was lined with epithelium and filled with a fluid in which floated masses of epithelial cells.

In the development of the thyroid gland we have the appearance of paired lateral portions which are united by an unpaired median portion. This latter, developed in conjunction with the root of the tongue, becomes elongated to form a duct, the upper end of which opens on the surface of the tongue. This duct, the ductus thyreoglossus, which is lined with ciliated epithelium, becomes interrupted at one point in the early stages of development, and at that point the hyoid bone develops. Thus the upper portion is cut off as the blind lingual duct and the lower portion as the ductus thyroideus. Frequently there stretches from the hyoid bone downward a series of small masses of thyroid tissue.

Cysts have been observed to arise from the lingual duct

<sup>1</sup> Kostanecki and Milecki, Virchow's Archiv, Bd. 120, 121.

<sup>2</sup> Verneuil, Archives Generales de Medecine, 1853, T. 91, p. 185.

and from the subhyoid portion. Even from portions of the obliterated duct enclosed in the hyoid bone similar cystic structures have been derived. Neumann<sup>2</sup> ascribes the origin of many cases of so-called Ranula to the cystic dilatation of portions of the lingual duct, the lining of ciliated epithelium being thus easily accounted for. When these lie above the mylohyoid muscles they project into the mouth. In the case described by Haeckel,<sup>4</sup> however, the tumor projected anteriorly in the median line of the neck. It proved to be a cystic mass lined by ciliated epithelium but containing in its walls definite thyroid gland substance. Its nature was therefore indubitable.

He concludes his paper with the statement that the thyroid can leave remains behind throughout the whole course from tongue to the neck from which ciliated cysts may arise.

M. Benno Schmidt, Roser, Chiari and others observed cases in which cystic tumors were found in the median cervical region, with more or less thyroid tissue in their walls and a lining of ciliated epithelium. All of these could readily be referred to the ductus thyroglossus as a point of origin.

This summary of the literature may throw light on the nature of the following case which occurred recently in the Johns Hopkins Hospital:

J. P., stevedore, aged 55, colored. Admitted on account of hemiplegia, presented a rounded swelling in the median line of the neck just above the thyroid region. He stated that it had been present as long as he could remember and that it had not increased in size nor given him pain or inconvenience. The tumor was regular in outline, smooth and rounded, and about  $4\frac{1}{2}$  cm. in diameter. It was not attached to the skin, which could be easily moved over it. Fluctuation could be felt.

The patient died after a second extensive cerebral hæmorrhage and at the autopsy the organs of the neck were removed *en masse* and sketched after dissection (Figs. 1 and 2).

The tumor proved to be a spherical unilocular cyst about  $4\frac{1}{2}$  cm. in diameter, with smooth rather thin wall. It lies upon and attached lightly to the sternohyoidei muscles, pushing them apart about  $1\frac{1}{2}$  cm. Vertically it reaches from the level of the isthmus of the thyroid to the level of the hyoid bone to the under side of the body of which it is most firmly attached, between the insertions of the above-named muscles. With the surrounding tissues and with the thyroid, the cyst is very slightly adherent and can be easily separated from them. On lifting it up the thyroid with its isthmus is plainly visible and seems quite normal. A narrow aberrant

band of muscle runs upward from the centre of the isthmus to the lower surface of the body of the hyoid bone.<sup>5</sup>

The walls of the cyst are about  $\frac{1}{2}$  to 1 mm. in thickness and are quite smooth. Blood-vessels are to be seen coursing over them. On opening the cyst it is found to contain a glairy mucoid fluid with a mass of cellular detritus which microscopically presents only very much disintegrated cells with deeply staining nuclear fragments. Cholesterol crystals were not seen.

The lining surface is quite smooth and velvety. The innermost layer can, however, be scraped off, leaving the dense white opaque outer layers of the wall.

Sections through the wall show it to be composed of a compact laminated connective tissue, which is somewhat looser in texture toward the outside. There is some adipose tissue on the outer superficial portions of the wall.

The lining cells form generally a single layer of high columnar ciliated epithelial cells (Fig. 3), but there are often nuclei and smaller cell bodies intercalated at the bases of these cells like those seen in various other surfaces covered with such epithelium. The underlying connective tissue very frequently contains groups of lymphoid cells but is in general composed of elongated fibrous elements. No thyroid tissue could be found in the walls.

It seems that such a unilocular cyst lying in the median line, connected firmly with the centre of the hyoid bone, and lined with columnar ciliated epithelium, must be interpreted as being derived from the ductus thyroglossus even although it is not directly or firmly connected with the isthmus thyroidea nor has any thyroid tissue in its walls. The nature of the epithelial lining eliminates the possibility of its being derived from the bursæ and there remain only the possibilities of a cyst derived from a hernia of the trachea and one derived from the entodermal end of a fistula of the 2nd branchial cleft. The median position and absolute lack of connection with either trachea or pharynx seem to rule these out and we must conclude that it represents those cysts which are developed from the ductus thyroglossus at that region where it extends from its attachment to the hyoid toward the thyroid.

The case was given to me for study by Dr. MacCallum, whose help in reviewing the literature, etc., I wish to acknowledge.

<sup>5</sup> Probably the Levator thyroideæ, first described by Soemmering, who named it Levator glandulæ thyroideæ. Streckeisen (Beiträge zur Morphologie der Schilddrüse, Berlin, 1886), states that it occurs in 79% of his dissections. Testut describes it as an aberrant bundle running between the hyoid bone and the sternum, but in some cases stopping in its course to attach itself to the anterior surface of the thyroid.

<sup>2</sup> Neumann, Langenbeck's Archiv, Bd. 33, S. 590.

<sup>4</sup> Haeckel, Langenbeck's Archiv, 1894, Bd. 48, S. 607.

## THE JOHNS HOPKINS HOSPITAL BULLETIN.

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FIG. 1.—Shows the position of the cyst as it lies over the trachea in the median line. The thyroid is seen projecting beneath it on both sides.



FIG. 2.—The cyst with the sternohyoid muscles is turned upward on its attachment to the hyoid bone; the isthmus of the thyroid is exposed, showing a thin median strand of muscle fibres which run upward toward the hyoid.

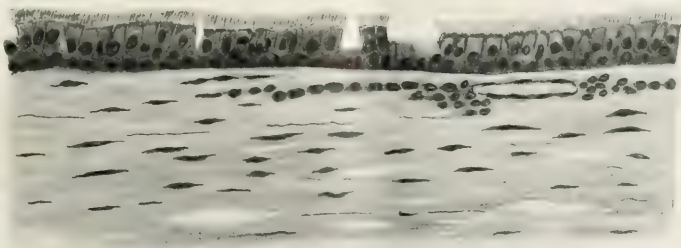
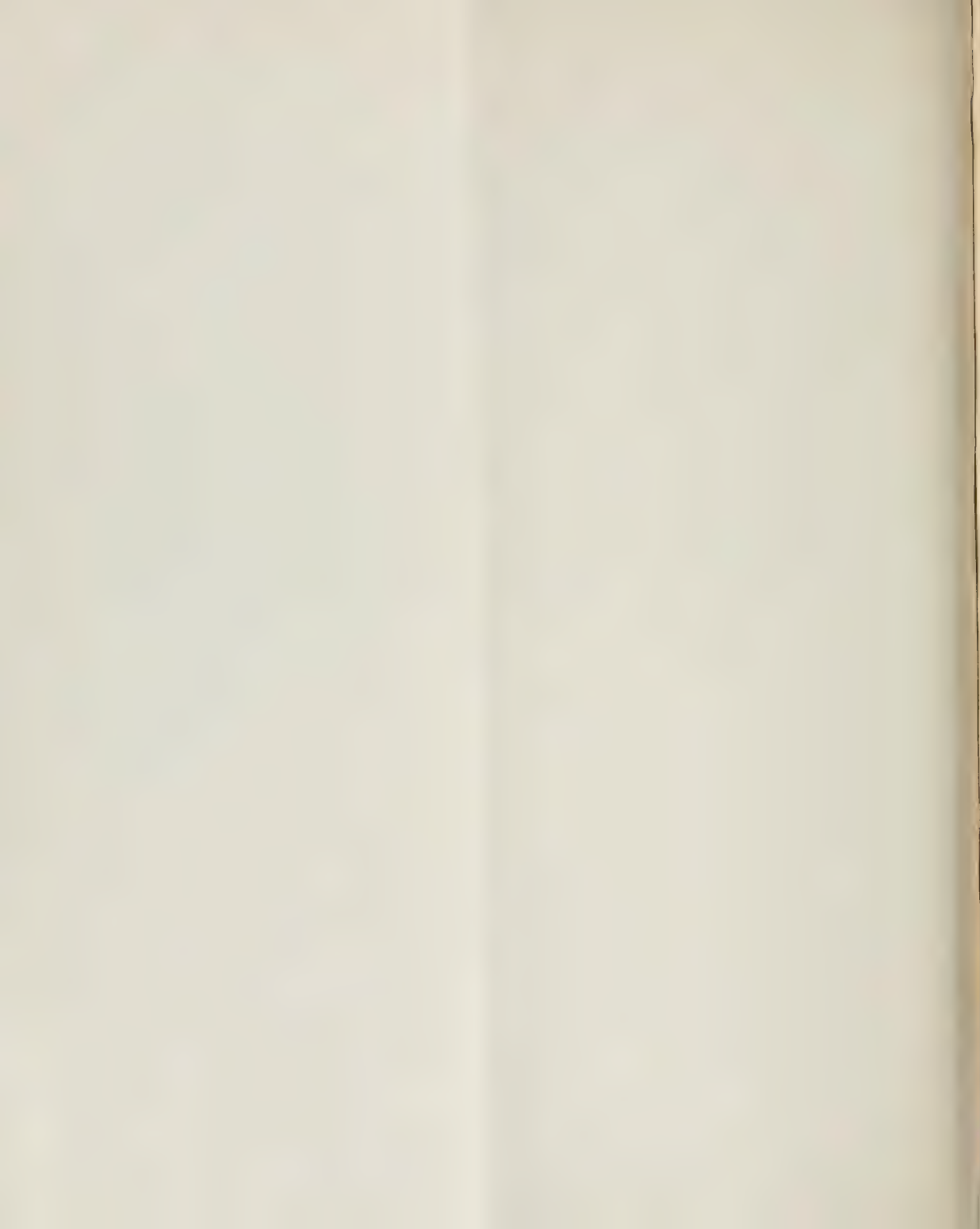


FIG. 3.—Section of the cyst wall showing the lining of ciliated columnar epithelium.



CATARRHAL OTITIS MEDIA (NON-SUPPURATIVE) AS A FACTOR IN THE ETIOLOGY OF FACIAL PARALYSIS.<sup>1</sup>

BY H. O. REIK, M. D.,

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I desire to call attention to what I believe to be a neglected factor in facial paralysis, a factor which, if I do not overestimate it, is of importance not only as a means of explaining the etiology and pathology of a large class of cases but of prime importance in determining the best form of treatment to secure the most satisfactory results.

Heuschmann, in the recent edition of Church-Peterson's *Diseases of the Nervous System*, is quoted as saying that in a series of 135 cases of facial paralysis he found 6 per cent due to injury, 9 per cent to ear disease and 75 per cent to be of the so-called rheumatic or refrigeratory type. In Mayer's translation of Oppenheim, 1900, it is stated that exposure to cold is the cause of 73 per cent of the cases of facial paralysis occurring in otherwise normal individuals. These figures are probably approximately correct, for all text-books on diseases of the nervous system, or on the practice of medicine, contain the statement that exposure to cold is the principal cause of facial paralysis. None of these authors, however, as far as I know, give a satisfactory explanation of the pathological process involved, and in every instance where disease of the ear is mentioned as an active factor in the production of such paralysis it is evident that the author was considering a suppurative otitis media with necrosis of the bony wall of the tympanum. From a consideration of the evidence which I shall here adduce I am convinced that in the majority of cases, if not indeed in all, of facial paralysis of the "refrigeratory or rheumatic" class, an acute or sub-acute otitis media is an intermediary condition between the exposure to cold and the appearance of the paresis.

Herter, referring to the pathology of this affection, in his article in *Nervous Diseases by American Authors*, says "it was formerly thought that exposure to cold caused facial paralysis by paralyzing the terminations of the nerve in the facial muscles. There is now good reason to believe that the affection always depends upon an inflammation of the trunk of the nerve (perhaps involving chiefly the sheath) within the Fallopian canal, and there is no evidence that inflammation ever involves the nerve after its emergence from the canal." This seems to dispose of the old theory of irritation of the peripheral nerve endings and also of the commonly accepted notion of a neuritis at some part of the trunk external to the stylo-mastoid foramen.

How shall we then explain the action of cold in the pro-

duction of facial paralysis? It seems to me a very simple matter if we but consider the anatomical relations of this nerve and bear in mind the very great frequency of acute or sub-acute otitis media following exposure to cold. It is an extremely common occurrence to hear persons who are suffering with a mild naso-pharyngitis complain of slight involvement of the ear, that is, a sense of stuffiness in the ear, perhaps accompanied by some deafness, and even at times a moderate degree of pain. These symptoms, evidence of a mild sub-acute otitis, pass away in a short time with the other features of the cold and no serious damage is done, but suppose such a condition in an individual whose facial nerve is exposed in its course through the middle ear, how much greater are the chances of a serious lesion?

As a matter of fact, dehiscence of the Fallopian canal in the tympanum is a very frequent anatomical condition; the upper half of the eminentia pyramidalis, a part of the canal wall, is under ordinary circumstances very thin and often presents deficiencies, so that it is not at all uncommon for the facial nerve sheath to lie directly in contact with the mucous membrane of the middle ear. Then, too, Zuckerkandl has called attention to the normal existence of a small foramen in the canal wall just above the oval window for the passage of a branch of the arteria stylo-mastoidea to the stapes. With an exudate in the tympanic cavity here is an excellent opportunity for direct extension of the inflammation to the nerve sheath, or, for the exercise of the baneful influence of pressure upon the nerve, and in this connection we must not overlook the differences in width of Fallopian canals, inasmuch as an exudate in a canal with narrowed lumen would produce paresis more easily than in a wide one.

The usual history of a facial paralysis occurring without any other apparent lesion in an otherwise normal individual is, that the patient having contracted a cold finds himself four or five days later, often earlier, with a drawn mouth, lagging eyelid, and soon, more or less complete inaction of the facial muscles of one side. He may or may not have had prodromic symptoms but, if he has, these generally consist of a pricking or stinging pain in the ear with a sense of stuffiness, slight deafness and tinnitus, following the ordinary symptoms of a cold in the head or sore throat, and preceding the first evidences of any trouble with the muscles. The ear symptoms are apt to be mild and sometimes attract so little attention that when the patient has become absorbed in the consideration of his more alarming condition, the

<sup>1</sup> Read before The Johns Hopkins Medical Society, December 2, 1901.

facial deformity, he forgets and, unless closely questioned, makes no reference to the previous ear trouble.

As illustrating these cases I might relate briefly the history of one which is typical of a series of four that I have personally observed.

Mr. T. W. McC. was brought to me for consultation by Dr. Clement A. Penrose on August 29. Five days previously he had first noticed signs of a right facial paralysis. He had been suffering slightly from a cold in the head accompanied by some pain, though not severe, in the right ear. There was no ear-ache at the time of his visit to Dr. Penrose but pressure over the mastoid elicited some tenderness along the anterior border of the process and over the antrum. The tympanic membrane was not congested but there were indications of fluid in the tympanic cavity.

A paracentesis was suggested and performed later in the day. When the membrane was incised there was a distinct ripping sound, heard by all in the room, like the cutting of parchment paper, showing that the membrane was on the stretch and under considerable pressure. This was followed immediately by the escape of several drops of serous fluid. A sterile cotton wick was inserted and the next morning this was found to be saturated with serum; the mastoid tenderness had diminished markedly and there was no pain, cedema or fever. No organisms were found. On the following day improvement in the paralyzed muscles began. The free discharge of serous fluid continued but at no time was there any appearance of pus. On the 29th the paralysis was complete on the right side, even of the orbicularis palpebrarum and the occipito-frontalis; August 31 he was able to close the upper lid to the lower edge of the pupil; September 1, upper lid margin could reach lower border of cornea and there was some movement of the brow; and by September 9 he had regained almost complete control of facial muscles. The discharge ceased within a few days and the perforation was almost healed when he left the hospital.

There can be, I think, little doubt that this was a case of mild pharyngitis, followed by a sub-acute otitis media, involving the mastoid antrum and perhaps other cells as well, which produced paralysis through the effect of the exudate upon the facial nerve in its course through the tympanum.

In support of this hypothesis I may bring up clinical evidence of a different character. It might be thought that as the majority of these cases get well in from one to four weeks without treatment, or under different forms of treatment, and at no time show any marked ear symptoms, that there is no good reason to suppose the middle ear involved. We know that the same good result is attained in the majority of untreated sub-acute middle ear catarrhs in which the nerve is not concerned and in either case the explanation is simple. In the more favored cases the exudate soon finds its way out of the tympanum through the eustachian tube and in the slower cases it is removed by gradual resorption; pressure relieved, the irritation of the nerve subsides and the muscles recover their function. Furthermore, the treatment found to be best adapted to the cure of these cases is very sugges-

tive of a relationship between the paralysis and middle ear disease. That which seems to have been agreed upon by all authorities as most beneficial is: the application of leeches over the mastoid, counter-irritants behind the ear, purgatives, and potassium iodide internally. These are precisely the remedies of most value in removing inflammatory products from the tympanic cavity—except where instruments may be employed.

The fact that I had, in my very limited experience, seen four cases of facial paralysis in which the middle ear was involved in a mild catarrhal inflammation just prior to the onset of paretic symptoms and which presented coincidentally a collection of fluid in the tympanum, the evacuation of which permitted prompt and rapid recovery of muscle power, led me to think that this pathological process might explain most, if not all, of the cases ordinarily described as "due to cold." I find that this point was suggested, however, as long ago as 1857 by Berard, and by Deleau, and that since then cases have been reported to illustrate this relationship by several writers. Tomka, in a very excellent article dealing fully with the subject of facial paralysis, in the *Archiv f. Ohrenhkl.*, April, 1900, emphasizes this point and reports other cases. The matter seems to have been generally ignored though and the indefinite statements of the numerous text-books excuse me for making this communication. This class of cases is of course rarely seen by the otologist and, unfortunately, the ear is very rarely examined by the family physician.

Now a word as to the bearing of all this on the treatment of facial paralysis. Admitting the natural tendency of the affection towards recovery and the beneficial influence of such treatment as has been referred to, we must still ask ourselves whether we can do anything more to hasten relief from the disability. I believe we can. If it be found that there is an exudate in the tympanum, the sooner it is removed the more rapid will be the recovery and, on the other hand, the longer it is allowed to remain there the greater will be the danger of permanent injury to the nerve. The easiest and quickest way to get rid of such an exudate is a paracentesis of the tympanic membrane and that is a simple and perfectly safe operation, not requiring any great amount of skill, and, if done under proper aseptic precautions, doing no harm even though it should be performed in a case where it was not needed.

The points I wish particularly to bring out then are these:

1. If exposure to cold, in one way or another, is the cause of most cases of facial paralysis, it probably acts most commonly through the production of an otitis media, whereby the nerve becomes involved either in a direct extension of the inflammatory process to its exposed sheath, or through pressure upon it of an exudate.

2. This being admitted, the form of treatment which offers the most rapid and satisfactory results is a paracentesis of the tympanic membrane to free the cavity of its abnormal contents.

3. We should never in any case of facial paralysis neglect to examine the ear.

## A NEW METHOD OF TEACHING THE MACROSCOPICAL ANATOMY OF THE CENTRAL NERVOUS SYSTEM.<sup>1</sup>

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We have recently introduced in the anatomical laboratory of the Baltimore Medical College what we believe to be a new method of teaching the macroscopical anatomy of the central nervous system.

The mother of invention, necessity, gave birth to this method. We have found it simply impossible to supply our large and ever-growing classes with sufficient neurological material to dissect. The brain from a cadaver cannot be hardened and consequently is useless for dissecting. We have to depend to a large extent on fresh bodies for our material; hence the supply is limited and precarious.

It is scarcely necessary for me to speak of the importance of practical laboratory work in the study of anatomy; especially is this true when one is studying the nervous system. There is nothing more conducive to knowledge than to actually work out the subject one is trying to master; on the other hand, there can be no doubt that the mere memorizing of facts in anatomy, presented almost entirely in lectures and text-books, furnishes the most certain means of forgetting them. The method I wish to speak of presents the subject to the student's mind in three different ways, stimulating his interest, and fixing his attention in such a manner that it is almost impossible for him not to understand his work, or forget it after once having learned it. After the student has finished dissecting (the head generally being the last part to be dissected) he begins the study of the brain by first reading over the subject in his text-book, and attending the lectures. He then studies the specimens contained in the glass cases (Fig. 1). These are prepared so that "he who runs may read." They are self-explanatory, each part of the brain being colored so that the student can locate the various structures without much difficulty. With each case there is a diagrammatic drawing, explaining the various colors. The cases (Fig. 2) were designed especially for this work and are made with heavy tin bottom and ends and glass sides and top. I wish to thank Dr. A. Tumbleson for valuable assistance in working out the coloring solutions for these specimens. They are made as follows:

Sol. No. 1. Make a thin syrup by dissolving brown shellac in alcohol.

Sol. No. 2. Dissolve refined caoutchouc in chloroform. Make a medium thick syrup.

Sol. No. 3. Take one part of No. 1 and add three parts of chloroform. This is done to thin the shellac and to prevent alcohol from precipitating the gum in No. 4.

Sol. No. 4. Add one part of No. 3 to two parts of No. 2, gradually stirring all the time. The solutions may be thinned with chloroform if necessary. They should be about as thick as honey. Then add the mineral colors, as chrome yellow, Prussian blue, raw umber, etc., and keep the solutions well corked. The brain is hardened in formaldehyde. The surface to be colored is thoroughly dried and the coloring matter applied with a brush. Allow this to dry and then immerse the specimen in preserving solution. This mixture forms a gummy covering, as it were, which does not penetrate the tissue, nor destroy the brain in any way, so that the same specimen may be used for other purposes, if necessary. The specimens are preserved in a weak formalin solution and last indefinitely.

After the student has finished studying these specimens carefully, and has formed some idea of the shape and location of the various structures, he then begins to mould the brain from his knowledge already obtained by the previous study, and now being put to a practical test (Figs. 3 and 4). Of course during this part of the work, students are allowed to refer to the original specimen and use every help necessary. It has been very gratifying to see the interest manifested by the students in this work. They all agree that after spending several hours in making a certain part of the brain, they are not apt to forget it very quickly. The advantage of this method is that it gives the student something tangible to work with. He does not have to form a mental picture of a structure he has never seen. It creates interest and enthusiasm, and as a result the student learns the anatomy of a part of the body generally conceded to be not only difficult, but oftentimes obscure.

<sup>1</sup> Read before The Johns Hopkins Hospital Medical Society, December 2, 1901.

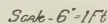


FIG. 2.—Working plan for making anatomical cases.

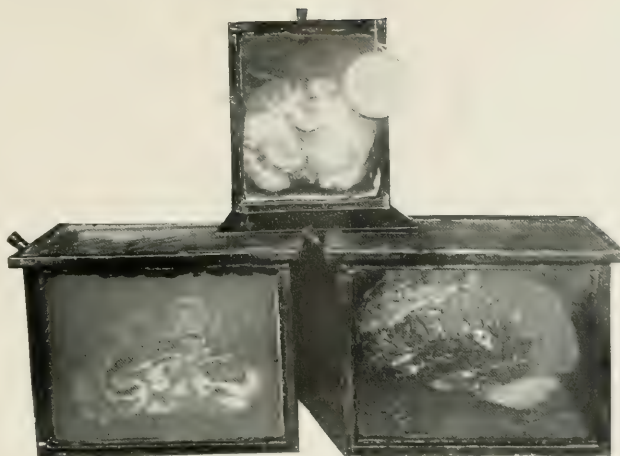


FIG. 1. Brains preserved and colored for study.

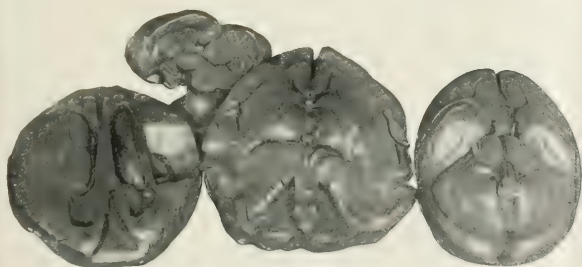


FIG. 3.—Models of brains made from clay

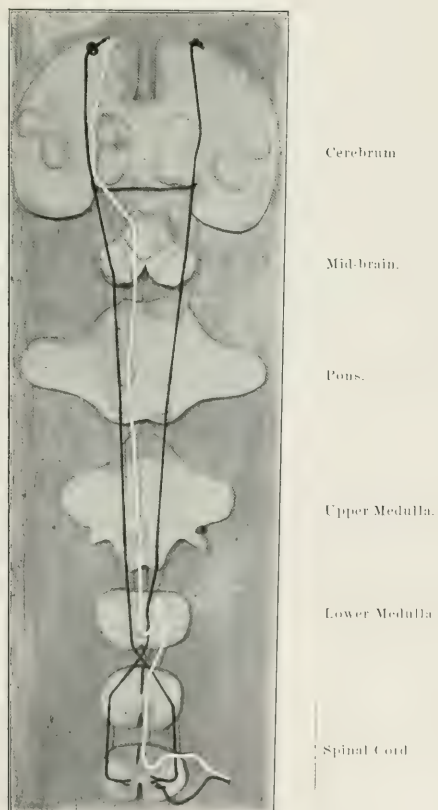
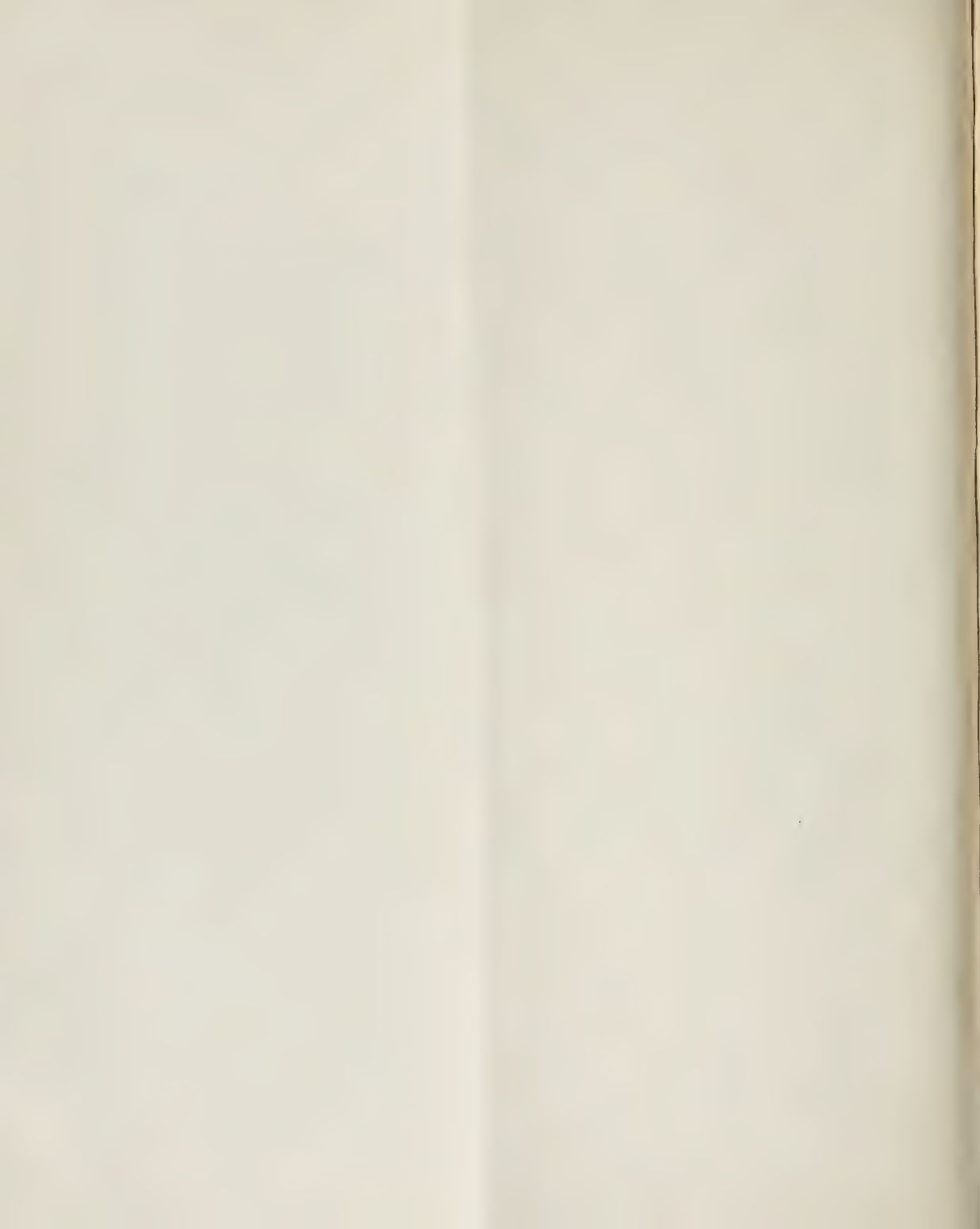


FIG. 4. Diagram of the motor (black), and sensory (white), tracts of the central nervous system.



SORCERY, MEDICINE AND SURGERY IN ANCIENT MEXICO.<sup>1</sup>

BY ZELIA NUTTALL.

We owe the greater part of our knowledge of native sorcery, medicine and surgery to the monumental work of Bernardino de Sahagun, a Spanish Franciscan friar of remarkable intellectual gifts, who went to Mexico soon after the Conquest and has left the most valuable work in existence on the customs and history of the Ancient Mexicans. An unpublished manuscript portion of this work preserved at the Royal Library at Madrid, where I studied and copied it in 1892, contains descriptions in the Nahuatl language of the various functions of what Dr. Seler of Berlin has rightly classified as sorcerers, fortune-tellers, jugglers and medicine-men.<sup>2</sup> A critical study of the passages relating to the so-called sorcerer reveals that his office was about the same as that of the "rain-maker" of the Pueblo tribes at the present day.

He is described as being a sorcerer, a prophet and one who can avert hail-storms. He knew the sky and the underworld, and could tell whether it would rain or not. He prophesied droughts and famines and directed the prayers and sacrifices which were to be made in order to avert these evils. He sometimes prophesied that frost was coming, or hail, or said: "in a year hence fire will fall upon us," a prophecy which in a volcanic country was probably associated with the idea of an eruption accompanied by showers of fiery ashes.

This type of prophet is described as a priest, who lived in strict seclusion in the temple and fasted. He alone had the power to protect the people from the evil sorcerers who, when animated by hatred, strove to destroy a village and its chieftain.

These evil sorcerers were generally named "tiacatecoloti," literally "owl-men," and are described as "those who do harm to others." It seems to have been the current belief that such a sorcerer could assume, at will, the form of an owl, and that by a mere look he could bewitch or "eat the life or heart of his victim." The sorcerer is finally described in the following text: "The man-owl, when he hates some one and desires his death, wounds him mortally and causes his possessions to be destroyed. He can make persons faint or become unconscious; he can cause darkness. Then he writes signs on the walls of the house. He wounds a person so that he lies down and then he wishes his death. But if any one can touch the sorcerer or seize him when he is in the house he becomes powerless and when dawn arrives he dies there, on the spot."

There were means, however, by which it was possible to protect a house from a sorcerer. A bowl of water, containing an obsidian knife, was placed behind the door or in the court-yard at night-time. When the sorcerer gazed into the bowl and saw his own reflection in it, crossed by the obsidian knife, he turned and fled and never ventured to return.

The power to rob their victims of consciousness is particularly ascribed to those sorcerers who, bent on robbery, made use of a potent charm, consisting of a dried human arm. These sorcerer thieves were known as the *tomamacpalitique*, a name which is recorded, in the singular, in Molina's dictionary, as meaning "a thief who steals and robs by means of enchantments or sorcery."

The following translation of Sahagun's description of the mode of procedure adopted by the sorcerer-thieves has already been published by me in an article on "Ancient Mexican Superstitions," which appeared in the *Journal of American Folk Lore*, Vol. X, No. XXXIX:

"They always chose for the exercise of their calling a day bearing the numeral nine, united to certain calendar signs which were considered particularly auspicious. Having decided to rob and plunder a certain house, they formed a band consisting of fifteen to twenty fellow-sorcerers, and manufactured an image of a serpent or of the patron of necromancy, *Quetzalcoatli*, the "Feathered Serpent." They then set out and danced towards the house, "that is to say, they advanced in unison, with measured steps, such as were executed in some of the old sacred dances. One of the leaders carried the aforesaid effigy, whilst a second carried over his shoulder the left forearm and hand of a woman which, according to certain superstitious beliefs, was supposed to possess the magical power of depriving persons of their senses. In order to employ this against the inmates of the house, the thieves first halted in its court-yard and struck blows upon the ground with the dead hand and then knocked with it at the threshold or lintels of the entrances. It was said that the effect of these ominous sounds caused the inmates of the house to fall into a profound sleep or swoon, and that they could not move or speak and seemed lifeless, although they saw and heard all that was going on. Some, however, actually slept, and even snored; whereupon the thieves lighted their torches, searched the house for provisions, and proceeded to enjoy a tranquil repast, the rightful owners observing them, spellbound. The robbers then ransacked the dwelling, took possession of every article of value it contained, tied these in bundles, and after committing other misdeeds, decamped and ran to their respective homes, laden with their booty. None of them rested on their way home; for it was said that if they did so they lost their power to rise again, and, being held spellbound until morning,

<sup>1</sup> Read before the Annual Meeting of the Baltimore branch of the American Folk-lore Society, April 26, 1901.

<sup>2</sup> In an article published in 1899, entitled *Zauberei und Zauberer im Alten Mexico* (Veröffentlichungen aus dem Kgl. Museum für Völkerkunde, Berlin), Prof. Ed. Seler published a good translation into German of the above mentioned portion of Sahagun's MS.

could be seized with their spoils and forced to betray their accomplices. In Dr. Otto Stoll's valuable and suggestive work on the rôle of suggestion and hypnotism in the history of psychology, he points out that the symptoms described above as produced by the talismanic knocks, are identical with those of suggestive catalepsy, aphasia, and hypnotism by suggestion. It can well be imagined that the mere fact of being aroused, under such terrifying circumstances by sounds proceeding from a talisman reputed to rob persons of the power of motion, may well have induced the conditions indicated by Dr. Stoll."

Sahagun also gives the following quaint version of a curious mode of enchantment employed by the native sorcerer named: "The setting up of a person in the fire." When the sorcerer has been much angered by any one and hates him, he makes his image in the form of a mummy and sets it up. He surrounds it with staffs decorated with paper flags. During four nights he manufactures these. He prepares food offerings and places them before the mummy, which he then burns during the night. He invites his victim to visit him at dawn and gives him the food offering which had been placed before the mummy. Whilst his guest eats it the sorcerer utters the words: "may you die soon."

In the same way "when a sorcerer has a grudge against a village, he goes to it and wanders about in the temple, in the house of the chieftain and of the people, wishing in his heart that all might be destroyed. When war breaks out he wishes that all may die in battle, and that the village may be converted into ashes. But when he is found out, when he is discovered, then he dies by the hand of the people then and there, or in his own house." It is evident from this that just as among the Pueblo Indians of the present day, an individual suspected of sorcery was exposed to losing his life. Sahagun also relates that there was a certain class of sorcerers who are called the "snake sorcerers or charmers," or "he who infuses life into snakes." These were consulted when any one had lost some property and suspected that it had been stolen from him. The following is a verbal rendering of Sahagun's quaint text:

"The sorcerer or snake charmer (who seems to have been somewhat of a juggler) was consulted in cases of theft. The complainant assembled the neighbors whom he suspected of having robbed him and the sorcerer made them all sit in a row on the ground. When all were assembled in the house he admonished them saying, 'My children, you are seated here because your neighbor is in trouble and because in my absence and in your absence some one has robbed him of his belongings. The guilty one had better return the stolen goods at once, because the sorcerer is now here and is about to identify him.'

"If, upon this, no one speaks and confesses his guilt, the sorcerer removes the lid of a bowl. When he has done this and has charmed the snake which lies in the bowl, it crawls out and looks around in all directions. It perceives the persons seated on the ground and looks at them, one after the

other. Then it crawls forward and confronts the people. When it recognizes the person who has stolen the goods it crawls upon him and lies on him. Then the others seize the guilty one and bind him and he confesses his guilt.

"If the snake sees no guilty person it returns to the bowl, coils up and quietly lies in it.

"In the latter case it was regarded as proven that there was no foundation for suspicion. The man who had been robbed just quieted himself and was satisfied."

The anonymous Hispano-Mexican MS. I discovered at the Biblioteca Nazionale Centrale in Florence and am about to publish under its title, "The Life of the Mexican Indians," contains an interesting illustration of what the text describes as "a kind of diabolical medicine which was practiced by the Indian women doctors."<sup>3</sup> It will be seen from the following text that this so-called diabolical rite was really no more than an attempt at prediction or "fortune-telling."

"When some one was ill they called the medicine woman or man in order to ascertain how the illness would end, and placed an idol in front of the patient. This idol was named Quetzalcoatl, or 'Plumed serpent.' A mat was laid upon the floor and the medicine woman placed herself on this and spread a white cotton cloth. She then took twenty grains of maize in her hand and cast them upon the white cloth, just as the Spaniards cast dice. If the said grains fell in a circle, leaving an empty space in the center, it was a sign that the patient would die of his illness and would be buried—the empty space being regarded as the sign for a grave. If the grains fell on top of each other it signified that the illness had been caused by sorcery or witchcraft, but if, in falling, the grains divided into two parts, one-half being on one side and one on the other, so that a straight line could be drawn through the middle of the group without touching a single grain, it was a sign that the disease would leave the patient and that he would recover."

After the preceding quotations, which afford a curious insight into the lives of the Mexican people shortly after the Spanish Conquest, let us now consult Sahagun's work about the medicine-men of ancient Mexico. One kind of medicine-man was designated as "he who takes something out of a person." The text reads: "When any one is ill he is called, so that he should remove the illness. He first chews a bitter herb named *iztauhiati*, sprinkles its juice on the person and rubs him over with it. Then he feels him all over. Wherever he finds a sore spot he removes from the flesh a pebble or an obsidian knife, a roll of paper or a splinter or something else. After he has done this some persons get well—others do not."

In the sacred books of the Quichés a historical medicine-man is recorded as stating that he "drew worms from the teeth or from the eyes."

Another class of healers is separately described as "he

<sup>3</sup> In Prof. Seler's article cited above, he published an unauthorized translation of this text, thereby anticipating my publication, the appearance of which has been unfortunately unavoidably delayed.

who sucks out illness," and the text relates: "When a child has a sore chest the sorcerer uses the herb *iztauhiati*, and sucks out blood or matter. Some children get well. Others do not."

An extremely curious mode of treatment for children is also given by Sahagun. "The child patient, or the patient child, was held head downwards and its head was shaken to and fro, its mouth being pressed close or stopped with cotton-wool. Of this prescription it may be surmised that some may have recovered, but that the majority did not."

While the above records appear to show that the medicine-man of ancient Mexico was identical with the North American Indian medicine-man of the present day, other details preserved show us that they also possessed remarkable knowledge of the curative properties of the native herbs. Indeed, old Spanish writers repeatedly refer to the remarkable knowledge of the medicinal properties of the native plants, possessed by the Mexicans and it is well known that, near Montezuma's palace, there was a garden in which medicinal herbs from all parts of the country were cultivated, for the use of the population of the City of Mexico.

The Mexican medicine-man had, moreover, likewise discovered the properties of certain plants and employed them as stimulants, in order to produce hallucinations, visions and ecstasy in connection with their religious rites.

We find that the native tobacco was used in this way. Its leaves were bruised and mixed with some alkaline substance such as lime or with charcoal. This paste was then formed into tiny pellets which seem to have been chewed or eaten and were carried by the priests in a small gourd or calabash, suspended from their necks. In the form of pellets tobacco was called "*ye-qualli*," "tobacco food," was designated as a "strengthenener or sustainer," and, like the coca of Peru, was used by those who set out on long, forced marches.

Dr. Seler, of Berlin, suspects that tobacco also formed the main ingredient of the so-called "divine food" employed by the Mexican priesthood which is described by Duran as having been a strange compound of all sorts of ingredients, such as dried and pulverized spiders, scorpions, etc.

While it thus appears that the ancient Mexicans principally chewed tobacco, we also know that they smoked it. In this case it was, however, prepared with great care and mixed with fragrant substances. The paste thus formed was introduced into a hollow reed, one end of which served as a mouth-piece. It was one of the refinements of ancient Mexican life to offer such "reed-tobacco" to guests, on small painted terra-cotta trays. We are informed that these fragrant reeds were usually smoked after banquets, and were considered a great luxury.

Whilst the ancient Mexicans thus appear to have made good use of the native weed, they also seem to have made an extremely intelligent use of other native products. Thus, in the treatment recommended for the preservation of the teeth, for toothache and inflamed gums, we find that char-

coal and the capsicum were used for the same purposes as in modern dentistry.

The following prescription for the alleviation of inflamed gums is a curious mixture of ignorance and practical common sense. I shall give it to you in literal translation:

"Inflammation of the gums is cured by lancing them with an obsidian knife and rubbing in a little salt with the finger. For toothache it is necessary to look for a certain kind of maggot and to grind it with some resin from the fir-tree. This is to be applied to the gum. Then heat a red-pepper or capsicum and press it and a grain of salt as tightly as possible upon the painful spot. Then lance the gum and apply a certain herb called *tlacacoatl*. If these remedies do not suffice, draw the tooth and put a little salt into the hollow place."

It is certainly interesting to find, in ancient Mexico, the employment of the primitive type of the modern capsicum toothache plaster and to realize that centuries of experience had taught the natives the value of the capsicum as a counter-irritant and of salt as an antiseptic.

It is likewise interesting to find the following cautionary paragraph in the old manuscript: "In order to avoid the above disease of the teeth it is well to avoid eating very hot food. If hot food is eaten, do not drink very cold water immediately afterwards. Always clean the front and back teeth after eating, also employ a wooden toothpick. Use cold water and salt for cleaning the teeth and rub them frequently with a cloth and some finely ground charcoal."

It is well known that the ancient Mexicans placed the highest value on the *temazcalli* or sweat-house as a curative agent, and I find it prescribed for all kinds of illnesses. It was resorted to by mothers immediately before childbirth, a custom still adhered to by Indian women in various parts of Mexico. The sweat-house was associated with the cult of the "earth-mother," the "grandmother of all," and many superstitious rites were associated with its use. The disapproval with which it was consequently regarded by the Spanish missionaries gradually restricted its hygienic usefulness. Its employment was accompanied by an intelligent use of massage, and we find that various forms of massage treatment were prescribed after the sweat-bath. Thus: "a swollen neck or sore throat is to be rubbed with the hand. A stiff neck or shoulder is to be pinched and squeezed." For a cough, however, the throat is to be rubbed with a finger only.

"Sprains are to be treated by rubbing very gently with the hand."

The treatment for headache is somewhat more heroic: "Smell a certain herb named *ecusco*, or the pepper plant when it is young and green. Tie up the head with a cloth and inhale the smoke of certain different kinds of incense. If the headache should get worse, pulverise the dry leaves of a certain herb named *cocoiatic* and use it as a snuff. If, however, the pain increases take some drops of the juice of a certain plant, mix these with a little water and sniff it up

the nose. If, after this, the pain is not allayed, take an obsidian knife and lance and bleed the head."

An insight into the mode of treating wounds is afforded by the following directions: "Wounds or cuts of the lip are to be sewn up with a human hair and then bathed with the juice of the agave plant. If, after the wound has healed, it leaves an ugly mark, it is necessary to re-open and burn it and sew it up again with a hair and cover it with melted ulli, that is to say, the juice of the India-rubber plant."

A peculiar mode of treating wounds is described by Friar Sahagun in a chapter devoted to the medicinal use of different stones, but I strongly suspect Spanish influence in these cases. It is, however, interesting to learn what ideas were prevalent amongst the Spanish missionaries in Mexico, about the year 1570.

had experience of the virtue of this stone, because I possess one which is about as large as a fist and is rough and uncut, just as when broken from the rock. In the year of 1576, during the pestilence of nose-bleeding, this stone saved the lives of many who, as the Chronicle quaintly says, "*were losing their blood and their lives through their noses.*" "On taking it into their hands and holding it tight for a while the nose-bleed ceased and they were cured of this disease of which many have died and still die in New Spain." The friar concludes with the statement that in the village of Tlatelolco of Santiago, there were many living witnesses of the above remarkable cures.

From Friar Sahagun we learn that, in cases of fractured bones, splints, made of pine wood, were used by the native surgeons. In conclusion, I will mention the existence, in



FIG. 1.

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FIG. 2.

Anonymous Hispano-Mexican Manuscript Entitled "The Life of the Indians," preserved at the Biblioteca Nagisuale Centrale, Florence, p. 58.

After describing the different kinds of obsidian the friar adds: "I believe that this stone is a kind of black emerald, as experience has taught me that it possesses particular virtues. When ground to a powder as fine as flour, and applied to open wounds or sores, it cures them very quickly and prevents festering."

"Catarrhs are cured, the voice is rendered clear, and internal heat is abated by taking two or three pills made by mixing powdered obsidian with quince cheese or some other thick preserve which absorbs a great deal of the powder." The friar states: In this country the blood-stone is also found, and it is green, with what look like drops of blood. This stone has the virtue of stopping the nosebleed. I have

ancient Mexican codices and manuscripts, of representations of two kinds of what we shall call, by courtesy, surgical operations.

One of these consists of the ceremonial piercing of the nostril of a warrior by an ancient Mexican priest, in order that he may wear the turquoise nose ornament, which was the equivalent to the Victoria Cross in Montezuma's time, and a mark of highest rank.

The pictures represent the warrior on the pyramid temple, resting his head on a kind of stone altar, while the high priest is piercing his nostril with the sharp point of an agave leaf (Fig. 1).

The second operation is that which was performed by the

high priest when sacrificing the lives of animals or human beings in the temples, and constitutes the most repulsive feature of ancient Mexican life. The native chronicles relate that the ritual sacrifice of human beings had only been in use for a comparatively short period in native history and had been adopted by the fierce Mexicans for the purpose of intimidating the tribes which they subjugated and forced to yield tribute. An extenuating circumstance is that only prisoners of war, slaves or criminals were thus sacrificed. Friar Duran gives a graphic description of the rite. The victim who had been drugged and was in an almost unconscious condition was placed with his back resting on the summit of a high conical stone. Assistant priests held his limbs and pressed them downwards, which caused his chest to protrude and to be at a high tension. The head priest then made a deep incision with a large flint knife which, as Duran crudely states, "caused the victim's chest to open like a ripe pomegranate." The priest then inserted his hand in the opening, drew the victim's heart, tore it out and held it aloft (Fig. 2).

A summary of the foregoing material seems to show that, whereas the ancient Mexicans had rain-makers and medicine-men, whose professional attainments were on a par with those of other American tribes of the present day, they also possessed an excellent knowledge of the hygienic uses of the sweat-house and massage and of the medicinal properties of various plants, and natural products, and put some of them to sensible and practical uses. Besides having acquired, through experience, a certain rudimentary knowledge of surgery, they also practiced upon human and animal victims by means of a stone knife, a form of operation which, although peculiar and extremely repulsive, appears to have been methodical and effective and to have demanded a certain amount of surgical skill and practice.

NOTE.—Original sources referred to: Fray Bernardino de Sahagun, *Historia General de las cosas de Nueva-España*, ed. Bustamante, Mexico, 1880, unpublished original texts. Fray Diego Duran, *Historia de las Indias de Nueva-España*, ed. Ramirez, Mexico, 1867. Fray Geronimo de Mendieta, *Historia Ecclesiastica Indiana*, ed. Icazbalceta, Mexico, 1870.

## PRELIMINARY NOTE.<sup>1</sup> THE EXTENT OF GASTRIC DIGESTION IN CASES OF CARCINOMA OF THE STOMACH.

BY CHARLES P. EMERSON, M. D.,

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(From the Clinical Laboratory, Basel, Switzerland, Prof. Fr. Müller, Director.)

At the suggestion of Prof. Müller a series of gastric contents were analyzed to ascertain if anything characteristic could be discovered in the progress of digestion in cases of carcinoma of the stomach, hyperacidity, and anacidity.

It has been recently shown by the Strassburg School that zinc sulphate may be used instead of ammonium sulphate to separate the various albumoses, hence the amount of albumoses in each fraction may now be easily determined by estimation of the nitrogen present. Using this method Zunz has shown that the chief end product of peptic digestion was not peptone, but that very early, even before any peptone was present, a considerable amount of nitrogen was in bodies between peptone and the amido acids (Pfaundler). This being the case, it is a point of considerable interest to ascertain if the per cent of nitrogen in albumoses, peptone, and these further bodies shows constant variations from normal in different diseases, especially carcinoma of the stomach, and whether these variations may be used in the early diagnosis of these diseases.

The method used is briefly as follows: a test meal, either the Ewald test breakfast, or, better still, fifteen grams of nutrose in four hundred ccs. of water, is given, and removed in one hour. The nitrogen of the neutralized and filtered

gastric content is first determined; the proto-albumoses are precipitated by half saturation, the deutero-albumoses by complete saturation with zinc sulphate; the peptone is precipitated by phosphotungstic acid, but since this reagent precipitates many other bodies also the term "P. W. precipitate" will be used instead of "peptone." The nitrogen of the filtrate after each precipitation is determined and thus the amount removed in the precipitate easily reckoned. The nitrogen in bodies precipitated neither by zinc sulphate nor by P. W. acid will be referred to as "nitrogen remaining." The results of these analyses is very interesting. In all conditions considered together except carcinoma the nitrogen was distributed approximately as follows: primary and secondary albumoses, 51.5 per cent; P. W. ppt., 31.4 per cent; remaining, 17 per cent. In carcinoma of the stomach, however, the figures were respectively, 25.22 per cent, 47.04 per cent, 27.74 per cent. That is, in carcinoma the digestion is more advanced, more of the nitrogen being present in those bodies beyond the albumose stage, than in the normal, hyperacid and anacidic stomachs.

This would confirm the opinion formerly held by Prof. Müller that in the carcinomatous stomach the carcinoma itself furnishes a ferment which aids in the peptic digestion. If this be the case, we should expect to be able to demonstrate its activity in artificial digestion mixtures. To show that

<sup>1</sup> Read before the Johns Hopkins Medical Society.

we can do this I give the results of one of my experiments on this point.

Two artificial gastric juices, consisting of water 500 ccs., hydrochloric acid (sp. gr. 1.124) 2 ccs., pepsin (Witte) 1.5 ccs., were made. To each was added fibrin 10 gms. To one, mixture A, was added 5 gms. of carcinoma tissue; to the other, mixture B, 5 gms. of the same carcinoma tissue which had been heated to 80° C. Tolnol was added to prevent bacterial growth. Analysis at the end of a few days in the thermostat at 40° C. showed:

	Mixture A	B
N. in albumoses . .	17.3 per cent	30.7 per cent
N. in P. W. ppt. . .	59.8 per cent	56.1 per cent
N. remaining . . .	22.9 per cent	13.2 per cent

Hence the presence of unheated carcinoma tissue in mixture A has resulted in a more advanced digestion than in mixture B. Similar results were obtained by experiments modified in various ways, omission of the pepsin and fibrin, of the fibrin, etc.

The recognition of the presence of a ferment supplied by the carcinoma will explain the early absence of free HCl in that disease, as the work of Stehelen on the bases of the gastric juice in carcinoma of the stomach, and of Rosenburger on the disappearance of free HCl from artificial digestive mixtures to which carcinomatous tissue has been added, both working under Prof. Müller's direction, will show.

In conclusion, I take the opportunity to emphasize the advantage of using nutrose or some other simple albumin as the test meal in such work. -Nutrose is a fairly pure casein preparation, is easily given (10-15 gms. in 400 ccs. water well salted or flavored with some non-nitrogenous substance), is easily removed, but what is more important, casein is more slowly digested, hence one can easily see variations in the progress of digestion.

A complete report of work on this subject thus far done will very shortly appear. The work is being continued with reference to the effect of various therapeutic measures on the digestion in cases of subacidity and hyperacidity, and especially to prove the value of the above point in the early diagnosis of cancer of the stomach.

#### DISCUSSION.

DR. J. C. HEMMETER.—The report impresses me as a resumé of the hypotheses attempting an explanation of why the carcinomatous stomach contains less hydrochloric acid than the normal stomach, and, then, an effort to establish one of these explanations on a more solid basis by chemical investigation. It is unfortunate (for the theory that the neoplasm gives rise to something which neutralizes the secreted HCl) that the carcinoma which originates from a gastric ulcer always has an excess of hydrochloric acid and yet, according to Hauser, it presents the architecture of typical carcinoma. It is an established fact that the excess of hydrochloric acid which is characteristic of gastric ulcer continues while the disease degenerates afterwards into a carcinoma. Then, too, it makes a great difference where the carcinoma is located. Hydrochloric acid is a product of well-defined histological elements in the peptic ducts, as proven by Langley, and Mall and Heidenhain. These oxyntic cells are limited to a particular zone in the stomach. If the carcinoma should originate where there are few of these cells it is logical to presume that it would not interfere so much with the formation of hydrochloric acid, as it would in a location where the oxyntic cells are normally abundant. So we are justified in considering that the explanation of absence of HCl in carcinoma rests upon this histologic basis, rather than upon the hypothesis that the carcinoma produces something by which the HCl is neutralized. Dr. Emerson has stated that the digestive experiments made with contents of cancerous stomachs carry the solution of proteids a little further than the normal stomach. It seems to me it is a too sweeping statement for there are carcinomatous stomachs that secrete no hydrochloric acid whatever, nor any trace of pepsin or rennin, nor the prozymogens of these ferments, and it is manifestly impossible for any proteolysis whatever to take place in such stomachs, excepting that due to bacteria.

I would like to ask if he has made any digestive experiments in which the contents were passed through a Pasteur filter, for it must be remembered that bacteria may play a very important part in these artificial digestion experiments, and bacterial proteolysis is considerable.

#### NOTES ON NEW BOOKS.

The Thirty-Second Annual Report of the State Board of Health of Massachusetts. (Boston: Wright and Potter, 1901.)

This report shows the work of the board for the year ending September 30, 1900. No changes in the membership of the board itself occurred during this year and the principal officers of the board also remained the same. The secretary of the board is Dr. S. W. Abbott; the engineer, Mr. X. H. Goodnough; the pathologist, Dr. Theobald Smith, the (food) analyst, Mr. A. E. Leach; the (water and sewage) chemist, Mr. H. W. Clark; and the consulting chemist, Dr. Thomas M. Drown president of Lehigh University; all men of the highest standing in their respective fields.

The general report points out a striking increase in the total

death rate of 1900 as compared with that of 1899 (18.24 per thousand against 17.40), and a great increase in infectious diseases. Thus, in 1899, 5855 cases of diphtheria were reported from twenty-six cities. In 1900, the same cities showed a total of 10,861 cases of this disease. Of eleven infectious diseases listed, five showed a decrease in deaths aggregating only eighty-seven, while the other six showed an increase in deaths aggregating fourteen hundred and eleven.

*Smallpox.*—During 1900 there were 104 undoubted cases (1899 showed 105), but in addition to these, 174 cases of doubtful diagnosis amongst which no deaths occurred were reported from New Bedford.

Statistics relating to the protection afforded by vaccination

are given, which are of interest in the face of the recent, almost pandemic, outbreak. One cannot but believe, in view of this and much similar evidence, that those who persistently oppose and evade vaccination, often by underhand measures, the garbling of evidence and even the outright manufacture of falsehood, must be misled, malicious or monomaniac.

*Typhoid Fever.*—Shows a slight decrease for the five year period ending 1900, the rate for this period being 2.4 per ten thousand inhabitants, against 3.2 for the previous five-year period.

*Consumption.*—Continues the fairly steady decrease heretofore shown, reaching 18.5 deaths per ten thousand in 1900.

*Diphtheria.*—Has already been referred to.

*Alleged Increase in Cancer.*—Investigation begun by the board on this subject has resulted in an exhaustive statistical report made by Dr. W. F. Whitney, who finds, in brief, that the increase is rather apparent than real and probably due to better diagnosis and registration, not to truly greater prevalence.

*New Legislative Acts.*—Of these, one forbidding the taking of shellfish from contaminated waters, and another, making the addition of preservatives to foods adulteration, are of interest as bearing on subjects recently much under discussion.

*Spring Waters.*—Notwithstanding the fact that Massachusetts has probably expended more time, energy and money on public water supplies than has any other State in the Union, over 91 per cent. of the population having access to such supplies, private owners of spring waters find ready sale for their special commodity. Over \$300,000 is spent annually by citizens of the State in this way. This is probably partly due to the fact that the surface waters of the State in general are more or less colored, during certain seasons of the year at least. In towns thus supplied, as well as in those where occasional bad odors or tastes (usually algal in origin) occur, the sale of spring water is highest. The board analyzed 99 of these spring waters; many of them proved excellent but in other cases, sewage contamination, old or recent, was quite evident.

*Water Supply and Sewerage.*—Much matter is given showing the advice of the board to many cities and towns regarding present or prospective systems, and the results of the analyses, chemical and microscopic, of the public water supplies now in use.

*Laurence Experimental Station.*—The work on sewage purification was directed to the further investigation of rapid methods of filtration, the handling of manufacturing wastes and certain problems relating to the septic tank. The conclusions arrived at seemed to be rather indefinitely stated.

Mr. Gage, biologist at this station, contributes a very interesting paper on actual tests of the efficiency of filters for each of various common species of bacteria; the persistence of *B. coli* and *B. typhi* in the filters after their application to the filters has ceased; and the comparative degree of purification achieved for bacteria in general, for *B. coli* and for *B. typhi*. Mr. Gage's results in brief were as follows:

The efficiency for each of various common species varied but little from the average general bacterial efficiency.

With an average general bacterial efficiency of 98.72 (filter 68) and 98.82 (filter 69), the *B. coli* efficiency was 99.86 and 99.81 respectively, the *B. typhi* efficiency 100 and 99.92 respectively.

*B. coli* persisted, after its application to the filter ceased, for two days in one case, seven days in the other.

*B. typhi* disappeared from the effluent of both filters promptly when application ceased.

*B. coli* appeared in the effluents more frequently than *B. typhi*, under approximately parallel conditions.

For these reasons and others, it is probable that *B. typhi* is a less hardy plant than *B. coli*.

On page 446, the presence of *B. coli* in the effluent of a filter as an indication of the harmfulness or innocence of the effluent is discussed in some detail. The tentative conclusion reached is that *B. coli* in such an effluent is not necessarily of serious significance.

*Bacteria in Ice.*—In 1888-89, the board began an investigation of certain Massachusetts ice supplies but were hampered in finishing the work by an almost total failure of the ice crop in the succeeding year. The subject was taken up again in 1899 and 1900 with results which tend to show that the carriage of infection through ice on theoretical grounds is not to be much dreaded. This conclusion was reached from experimental consideration of the physics of freezing in natural and artificial ice. The crystallization tends to throw out of the ice, as it forms, substances, both in solution and in suspension, present in the water. Ninety per cent and upwards of the bacteria in the water are thus thrown out physically, when ice freezes from the top and not entirely to the bottom. Should the ice "freeze solid" to the bottom, as in shallow ponds or in artificial manufacture, the bacteria expelled from the first ice formed would of course be included in that formed at the end of the process.

Two other factors of safety in preserving ice, natural or artificial, from bacterial infection of sanitary significance, elucidated by the work of Winslow and of Park, were not given, the writer thinks, sufficient weight in arriving at the conclusions. These factors are (1st) the dying out of typhoid bacilli in the water at the temperature just above 0° C. necessarily preceding freezing, to the extent of not less than 90 per cent of the total number in the water originally, and (2nd) the dying out of typhoid bacilli in the ice itself, also to the extent of not less than 90 per cent of the numbers actually included in the ice, within a short time after freezing. Thus, one million typhoid bacilli per cc. introduced into a pond on the point of freezing would be usually reduced to 100,000 before any ice which could include them would be formed. Of this number but 10,000 would escape physical expulsion from the ice and only 1000 of these would survive twenty-four hours' sojourn in the ice itself. This degree of purification, 99.9 per cent, is as high as that attained by the best sand filter in existence. Moreover, this figure is calculated on the basis of 90 per cent reduction at each stage. Inasmuch as much higher degrees of reduction are often attained especially if the time limits be prolonged, as they usually are, where natural ice is in question, it is easy to see that the possibilities of infection through ice even under conditions favorable to such infection are very slight. It is scarcely too much to say that a deliberate attempt to introduce typhoid fever into a community through the medium of a natural ice supply would usually fail of its object. If this be true, infection occurring without deliberate aid can rarely exist.

*Food and Drug Inspection.*—Mr. Leach continues in the report of his department for this year the excellent plan, pursued in one or two previous reports, of describing in detail the methods used both chemical and microscopic. He adds a special report on the distribution of arsenic in wall papers, dress goods, etc., and also on the presence of chromium in black stockings. Several cases of poisoning from these sources were traced by the board. The presence of arsenic is usually associated in the lay mind with green colors because it was at first much used in the making of Scheele's and other arsenical greens. These colors are less used than formerly, however, and arsenic is found rather as an impurity incidental to the manufacture of various dyes or as an ingredient of certain

reagents used in the manufacture of cloth, as for instance, in sizing solutions, to which it is added for antiseptic purposes. As an example of the injury done, a red plaid gingham made into a dress for a child four years old produced apparent poisoning the first day the dress was worn and on analysis 1.024 grains of metallic arsenic per square yard were found.

It is noteworthy that the chromium in black stockings is quite insoluble in boiling water and cannot be removed in this way; nevertheless, it seems that the perspiration, especially that of certain persons, acts as a solvent on the chromium salts; certainly some persons are more susceptible than others to such poisoning. It is perhaps necessary also that a slight abrasion of the skin should exist.

The report concludes with the usual record of antitoxin made and the diagnostic work carried on under the control of Dr. Theobald Smith, statistics of cancer in Massachusetts, statistical summaries of disease and mortality and the health of towns, which latter include investigations made by the medical inspector of the board, Dr. Morse.

In typography, arrangement and matter, the annual reports of this board have been familiar for years to all hygienists as standards of excellence, and the present report will do nothing to injure this reputation.

HIBBERT WINSLOW HILL.

Text-Book of Histology. Including the Microscopic Technic.

By Dr. PHILIPP STÖHR, Professor of Anatomy at the University of Würzburg. Fourth American based upon the Ninth German Edition. Translated by Dr. EMMA L. BILLSTEIN, formerly Director of the Laboratories of Histology and Embryology, Woman's Medical College of Pennsylvania. Edited, with additions, by Dr. ALFRED SCHAPER, Professor of Anatomy, University of Breslau; formerly Assistant Professor of Histology, Harvard Medical School, Boston. With 379 illustrations. Octavo, 500 pages. (*Philadelphia: P. Blakiston's Son & Co., 1012 Walnut St., 1901.*) Price \$3.00 net.

On picking up this fourth American edition of Stöhr's histology, our attention is arrested by its considerable increase in weight over the German edition. Such an increase we can hardly consider an improvement.

We are surprised not to find an editor's preface to this edition. The body of the book is exactly the same as the third edition. The revision consists of an appendix at the end of the book, an exceedingly clumsy and inconvenient method for the reader. We are very much surprised to find in this appendix, which is the second one the book contains, that many of the illustrations are duplicates of those in the body of the third and fourth editions, so while the title page is correct in intimating that there are 78 more illustrations than are found in the third edition, it gives the wrong impression that all of these are new.

One asks the occasion for such an edition and on whose responsibility it was undertaken. It may be that the recent American edition of an excellent German histology has proven a stimulus to the edition under consideration.

While in the main we can recommend Prof. Stöhr's histology, we cannot approve the methods adopted in bringing out the fourth American edition.

Transactions of the Medical Association of Georgia. Fifty-Second Annual Session, 1901. (*Atlanta, Ga.: Published by the Association, 1901.*)

This volume of transactions indicates an excellent degree of activity in the Medical Association of Georgia. The papers, as a rule, are well presented, practical and in full accord with modern ideas. The discussions reveal more or less difference

of opinion. The old straw as to the existence of hydrophobia is once more thrashed over, and several apparently able physicians are arrayed upon the negative. One would think that by this time the most sceptical would be convinced of the existence of the disease. A paper entitled "A new discovery in the treatment of chronic diseases dependent upon cell changes," presented by an Atlanta physician, should not have been published. We have no reason to think that the "Roberts-Hawley Lymph Compound" will ever be official or even heard of among reputable physicians. The author had no right to exploit a private proprietary remedy in the Association and the Association should not endorse it, at any rate without a full knowledge of the character and action of the remedy.

The Pathology and Treatment of Sexual Impotence. By VICTOR G. VECKI, M.D. Third edition, revised and enlarged. (*Philadelphia and London: W. B. Saunders & Co., 1901.*)

The author of this little book has written a scientific treatise upon an important and much neglected subject. The chapters upon the anatomy and physiology of the sexual organs probably contain nothing new, but the work of compilation is judiciously done. The succeeding chapters on the etiology of impotence, forms of impotence, and treatment are the most important. The author takes a sensible view of the mooted question of "frauding" and believes that its injurious influence upon both sexes has been much exaggerated. The treatment of impotence in general and of sexual neurasthenia is discriminating and judicious. Like many other neurologists the author believes that in some cases of sexual impotence good results are often obtained by hypnotism; in fact he regards it as an indispensable remedy in psychical impotence.

Medical and Surgical Reports of the Boston City Hospital. Twelfth Series. Edited by HERBERT L. BURRELL, M.D., W. T. CONNOLMAN, M.D., and CHARLES F. WITHERINGTON, M.D. (*Boston: Published by the Trustees, 1901.*)

A most interesting and valuable paper in this series is the report upon 949 cases of pneumonia treated in the City Hospital between the years 1895 and 1900 inclusive. Of these 949 cases 341, or 35.9 per cent, died. This seemingly large death rate was ascribed to the fact that all cases who entered the City Hospital in a moribund condition were included but all mild cases who may have entered after the crises, or when the physical signs had disappeared, were eliminated, as also all children younger than fifteen years. The observations which have been made upon the complications of pneumonia are also of exceeding interest. We are somewhat surprised that ten cases of phlebitis had been observed and that one patient only had died. The number seems large and the mortality small. No mention is made of venous thrombosis in the same connection.

About the only contribution to medical treatment in the article is the numerical demonstration that treatment by means of baths shows a slight percentage against the utility of the bath, as probably might have been expected. The do-too-much treatment seems a shade worse than the do-nothing treatment in pneumonia.

The volume contains sixteen monographs upon various medical, surgical, gynecological and pathological subjects, some of which are of extreme interest and all are valuable.

Dose-Book and Manual of Prescription-Writing: with a List of the Official Drugs and Preparations, and the more important Newer Remedies. By E. Q. THORNTON, M.D., Demonstrator of Therapeutics, Jefferson Medical College, Philadelphia. Second Edition, Revised and Enlarged. Octavo, 362 pages, illustrated. (*Philadelphia and London: W. B. Saunders & Co., 1901.*)

As a careful review of the former edition appeared in Volume VI, of the BULLETIN, little needs to be added except the statement that extensive additions have been made to the present edition, which materially increase the value of the book. The book can be recommended both to students of medicine and practitioners as full of practical and useful suggestions.

Golden Rules for Diseases of Children. By GEORGE CARPENTER, M.D. (Lond.), M. R. C. P. "Golden Rules" Series No. XI. (Bristol: John Wright & Co., 1901.)

This is another of the little books published by Wright & Co., which contains much useful information in small compass. The precepts inculcated are excellent. One regrets, however, that the limits allowed by the publishers leave so much unsaid.

Mosquito Brigades and how to Organize them. By RONALD ROSS, F. R. C. S., D. P. H., F. R. S., Walter Myers Lecturer on Tropical Medicine, Liverpool School of Tropical Medicine. (New York: Longmans, Green & Co., 1902.)

The object of this attractive little volume of just 100 pages is to show how war can be most effectively waged against mosquitoes. It treats of things to be learnt and things to be done. Among the former are certain elementary facts which in his judgment underlie the whole mode of warfare. He declares, for example, that all mosquitoes breed in stagnant water; that the variety known as *Culex* convey elephantiasis and yellow fever; that the variety known as *Anopheles* carry malarial fever; that the former bite by day and by night and that the latter bite mostly at night; that the larvæ of all mosquitoes require at least six or seven days' life in water before they reach maturity; that adult mosquitoes may live for months even in captivity, hibernating in cold climates and resisting severe frost or severe heat; that where mosquitoes abound in a house larvæ may usually be found within a short distance and that in the great majority of cases, especially in towns, almost every house breeds its own mosquitoes in its back yards or in puddles and drains in the streets close by. If these facts are true the object of a mosquito brigade should be not to exterminate mosquitoes in any entire continent but in the town in which we live and in its suburbs. This involves not killing every mosquito even in this town but destroying as many as possible, and above all, preventing mosquitoes from breeding in the town itself.

To accomplish these ends by concerted action, houses, back yards and gardens should be cleared of all rubbish, cisterns and tubs containing larvæ should be emptied and the larvæ destroyed. Pools, ditches, wells and puddles should be drained or filled up, and, if nothing more can be done, larvæ should be destroyed periodically with oil or by brushing them out with brooms or by other means. The motto should be, no stagnant water. Very sensible directions follow for the organization of mosquito brigades and for destroying the malarial organisms both within and without the animal body.

The book is capitally written in a vein of genial cynicism born of ineffectual effort to get municipalities to act promptly and efficiently in sanitary matters. It should be widely circulated and mosquito brigades should be established in every town. The author's remarks upon Koch's suggestion to cinchonize whole communities to destroy the malarial organisms already present in the human body seem very sensible. He regards such a proceeding unwise and unnecessarily expensive.

Typhoid Fever and Typhus Fever. By Dr. H. CURSCHMANN, Professor of Medicine, Leipzig. Edited with additions by WILLIAM OSLER, M.D. (Philadelphia and London: W. B. Saunders & Co., 1901.)

This is the first volume to be published of the English trans-

lation of Nothnagel's System of Practical Medicine. It is not necessary to say how much this will be welcomed. To many of the profession a foreign treatise is in very fact a sealed book. To those familiar with German medicine there is no need of reference to the position of Professor Curschmann. He is a recognized authority. In the editing of this volume Dr. Osler has drawn largely from his own experience of typhoid fever, specially from his service in this hospital, where, under his direction, the disease has been systematically studied. Where new material has been added this has been done so that it reads with the original text. The advantage of this must be at once evident on reading the book, and it is to be hoped that the editors of the other volumes will do likewise. The translation is good and the text reads smoothly and well.

About three-quarters of the work is given to typhoid fever and the remainder to typhus fever. The discussion of typhoid fever opens with a section on the etiology. This is complete and as elsewhere there is satisfactory description of the bacteriology. Attention is to be drawn to the summing up of the main points in the form of conclusions at the end of the section. This gives in less than two pages more about the disease than could be considered possible. It must be read to be appreciated. Following this is the section on pathology, which includes both the post-mortem findings and the clinical features. Here again attention must be drawn to an admirable general description of the disease which opens the section. In less than eight pages is given a picture of the disease not surpassed anywhere. One wishes that there were more medical writers who had this power of saying much in few words. The post-mortem findings are described fully and the author then takes up the symptoms and complications. To these of necessity a large space is given. It is not possible to note the divisions in detail, but those dealing with hæmorrhage and intestinal perforation are specially worthy of note. The question of the early diagnosis of perforation is discussed fully. The importance of an accurate knowledge of this complication can not be overestimated. The author lays special stress, and rightly so, on the importance of abdominal pain in this connection. Attention may also be called to the description of the features in the nervous system. But there are so many sections which are worthy of notice that choice is difficult.

Under treatment, the author speaks, of course, for the use of baths. We are glad to note that he considers the use of water at a temperature lower than 70° rarely necessary and advises usually water at a temperature of 78°. This coincides with the experience of this clinic where the ordinary bath temperature is 75° or 80°. He uses but few drugs and these usually quinine, antipyrine and phenacetine, with a preference for the first named.

The same excellent features are found in the discussion of typhus fever. Throughout the whole work there is so much that is admirable that selection is not easily made. It is to be commended most highly and should be read by every student of the diseases of which it treats.

A Text-Book of Diseases of Women. By CHARLES B. PENROSE, M.D., Ph.D., formerly Professor of Gynecology in the University of Pennsylvania. Fourth Edition, Revised. Octavo volume of 539 pages, handsomely illustrated. (Philadelphia and London: W. B. Saunders & Co., 1901.)

A full review of the first edition of this work appeared in the BULLETIN, Volume IX. The third edition contains an interesting synopsis of the author's experience in 310 cases of suspension of the uterus, in 211 cases of which he has been able to follow the subsequent history. Several of the illustrations

of cancer of the uterus have been replaced by better ones and the danger of transplantation of cancer cells into healthy tissue during an operation is pointed out. Werder's operation is also described. A paragraph on senile endometritis has been added. Several excellent illustrations of tubal pregnancy have been adopted from Kelly's Gynecology and a good illustration of a corpus luteum cyst has been incorporated. Primary carcinoma of the ovary is granted a more lengthy consideration. We are very glad to see the use of rubber gloves recommended in abdominal operations but surprised to learn that catgut should be avoided "within the peritoneal cavity," particularly since we now have such sure methods of sterilization as have been proved by bacteriological examination. We also regret to see the glass drainage tube, now a relic of the past, advocated. On page 507, under the heading of Marsupialization, we are told that in some cases where the cyst is densely adherent it should be evacuated

and brought to the abdominal incision. "Vegetations, etc., should be removed from the interior of the cyst with the fingers. The opening in the cyst should then be attached to the lower angle of the abdominal incision." It is now well known that the walls of ovarian cysts are composed of lamellae of connective tissue and that the inner or secreting layers may be peeled off, leaving merely the outer shell of connective tissue with its surrounding adhesions. The cavity remaining, in favorable cases can be obliterated with catgut or, if necessary, it may be drained for a short time. The secreting cyst surface is thus removed at once and not left in situ as the author advises. In conclusion we can merely repeat what was said of the first edition, the illustrations both of the gross and microscopical specimens are well executed and the text concise and clear. The book was written for students and to them it can be recommended as one of the best we possess.

T. S. C.

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# BULLETIN

OF

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### THE EFFECT OF CERTAIN POISONS ON INORGANIC FERMENTS.

BY HARRY C. JONES, PH. D.

*Associate Professor of Physical Chemistry, in The Johns Hopkins University.*

A brief review of the work of Bredig and his pupils on Inorganic Ferments has already appeared in this BULLETIN.<sup>1</sup> This work has been continued and some striking relations between the inorganic ferments and certain enzymes have been established.

The inorganic ferments in question are finely divided metals, such as platinum, gold, silver, cadmium, etc. The metals are obtained in the finely divided condition by dipping bars of the metal in question into pure water, and passing a heavy electric current from one bar to the other through the water. The metal under these conditions is torn off in a state of such fine division that it remains suspended in the water in the form of a solution. Indeed, the metal is in such a state of division that the most powerful microscope fails to reveal any heterogeneity when a drop of the solution is brought beneath it. From this it might be concluded that these solutions of the metals are true solutions. Such, however, is not the case. True solutions freeze lower than the pure solvent, have less vapor-tension or boil higher than the

pure solvent, and exert osmotic pressure. The solutions in question of the metals have none of these properties. They have the same freezing-point, the same vapor-tension or boiling-point as the pure solvent, and do not exert any osmotic pressure. To distinguish these solutions of the metals from true solutions they have been termed *pseudo-solutions* or *colloidal solutions*.

These are in no sense a new class of solutions. Examples of colloidal solutions have long been known. Solutions of starch, albumen and the like are as truly colloidal solutions as those of the metals in question. The solutions of the metals, however, have certain remarkable properties which seem to resemble in many respects the properties of the organic ferments. Some of these were referred to in the earlier review. It was noted that a colloidal solution of platinum accelerates the oxidation of alcohol to acetic acid in the presence of the oxygen of the air, as well as the organic ferment *mycoderma aceti*.

Finely divided iridium decomposes calcium formate into calcium carbonate, carbon dioxide and hydrogen in the same manner as certain bacteria.

<sup>1</sup> The Johns Hopkins Hospital Bulletin No. 114, September 1900, p. 224.

The analogy between the action of the finely divided metals and ferments was not limited to fermentation proper, oxidation, etc.; but held also for diastatic phenomena such as the inversion of cane sugar. The finely divided metals effected the inversion of cane sugar in a manner which was strictly analogous to the action of invertase.

Again, hydrogen dioxide was decomposed into water and oxygen in exactly the same manner by the colloidal solutions of the metals as by the ferments in the blood.

Many relations similar to the above were pointed out by Bredig and von Berneck,<sup>2</sup> in the first communication on this subject. These relations are, however, purely qualitative, and alone are entirely insufficient to establish any deep-seated connection between the action of the finely divided metals on the one hand, and organic ferments on the other.

The first investigation was a quantitative study of the action of the colloidal solutions of the metals as compared with the action of organic ferments. As this has already been reviewed, a brief reference to the conclusions reached by Bredig and von Berneck is sufficient.

It was shown in the first place that very small amounts of metal can effect the decomposition of enormous quantities of hydrogen dioxide, just as very small amounts of organic ferments can effect relatively large transformations. This analogy is, however, not necessarily very striking.

It was then shown that the finely divided metals do not enter into the reaction which they effect. The method by which this was proved was considered at sufficient length in the earlier review.<sup>3</sup>

Substances which behave in this manner, *i. e.*, act by means of their surface alone without entering into the reaction, are known as *Catalyzers* and such reactions are termed *catalytic*. The colloidal solutions of the metals, then, act catalytically. It is also well known that enzymes act catalytically. They do not enter into the reaction as such, but act simply by contact through their surface.

This analogy between the action of the colloidal metals and the enzymes is much closer than that first referred to, and makes it probable that the relations between the two are really deep-seated. There is, however, a relation far more striking than either of those considered above.

It is well known that the enzymes are very sensitive to certain substances, which, in infinitesimal quantities, may retard or entirely prevent their action. Thus, hydrocyanic acid, carbon bisulphide, hydrogen sulphide, and the like, when present in mere traces, may interfere seriously with the action of certain ferments. It has been shown that the merest trace of substances like the above may seriously interfere with the action of the colloidal solutions of the metals—may *poison* the finely divided metals. It is with this subject that the present review has to deal directly.

In their first paper certain qualitative observations were made by Bredig and von Berneck on the poisonous action of a few substances on colloidal solutions of platinum. This

subject has subsequently been studied quantitatively by Bredig and Ikeda.<sup>4</sup> They have worked with colloidal solutions of platinum, and have studied the rate at which these decompose hydrogen dioxide. Solutions of certain poisons of different concentrations were added to the colloidal solution of platinum, and the rate determined at which the colloidal solution, after it had been poisoned, decomposed hydrogen dioxide.

The velocity of the decomposition was found to diminish when the poison had been added to the colloidal solution, and the amount of diminution depended upon the amount of poison present. The diminution in the velocity was worked out numerically, but the results can be seen most readily by means of curves.

Fig. 1 represents the results obtained with hydrocyanic acid as the poison. The abscissa represents the time during which the reaction has proceeded. The ordinate, log

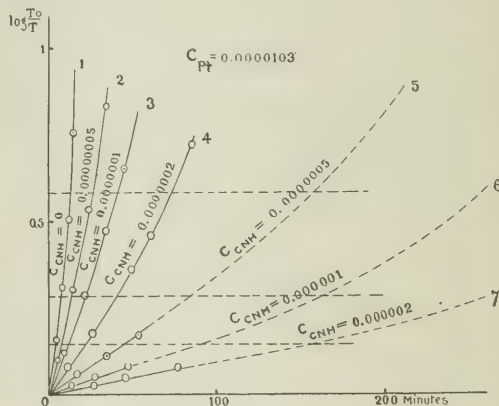


FIG. 1.—HYDROCYANIC ACID.

$\frac{T_0}{T}$ , is really  $\log \frac{A}{A-x}$ , in which  $A$  is the amount of the hydrogen dioxide originally present and  $x$  the amount decomposed. Without going more fully into this expression it may be stated that it is obtained by integrating the equation for a first order reaction derived from the law of mass action.

The concentration of the colloidal solution of platinum which was used,  $C_{Pt}$ , contained 0.0000103 of a gram-atomic weight per litre. The concentration of the hydrocyanic acid which was employed,  $C_{HCN}$ , expresses the number of gram-molecules of the acid in a litre of the solution.

Curve 1 represents the reaction when no poison is present. Curves 2 to 7 represent the reactions when increasing amounts of the poison were present. Take curve 5. Here the reaction velocity has been reduced to about one-half, and this has been effected by a solution of hydrocyanic acid containing one gram-molecular weight in two million

<sup>2</sup> Ztschr. phys. Chem. 31, 258, (1899.)

This BULLETIN, 114, 225, (1900.)

<sup>4</sup> Ztschr. phys. Chem. 37, 1, (1901.)

litres. Such a solution contains in a litre only 0.014 milligrams of hydrocyanic acid, and yet is capable of diminishing the action of the colloidal platinum to one-half.

Curves 4, 3 and 2 represent decreasing amounts of the poison as expressed by the values of  $C$ . Curve 2 represents the effect of a solution of hydrocyanic acid so dilute that it contains *one gram-molecular weight in twenty million litres* of the solution; and at such inconceivable dilutions the action of the platinum is considerably lessened.

It has been found that the action of the enzymes in the blood in decomposing hydrogen dioxide is very appreciably lessened by the addition of a solution of hydrocyanic acid containing 0.002 milligrams in a litre.

A careful examination of the curves brings out another very interesting relation. The curves for the most dilute

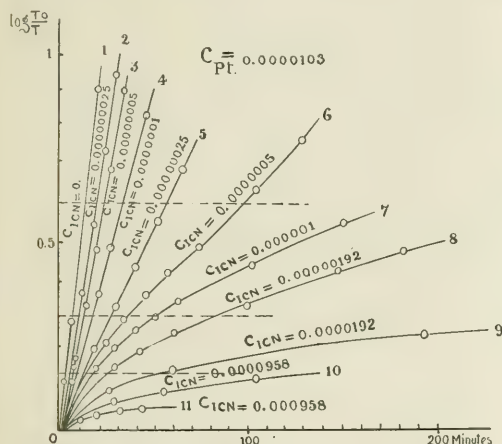


FIG. 2.—CYANOGEN IODIDE.

solutions of hydrocyanic acid are convex to the abscissa from the very origin. This means that the poison is having less and less effect as the time increases—the colloidal solution of the platinum is *recovering from the poison*.

Where the solution of the hydrocyanic acid is stronger (curves 5, 6 and 7) the curve is at first concave to the abscissa, and becomes convex only after a much longer time has elapsed. While the curve is concave to the abscissa the action of the poison is increasing, and the platinum begins to recover from the effect of the poison only after a much longer interval of time.

Similarly, it has been shown that the enzymes in the blood and ferments can recover from the poisonous action of minute traces of hydrocyanic acid.

It is pointed out that both of these effects are probably due to the oxidation of the hydrocyanic acid in the solution.

A more violent poison than hydrocyanic acid is cyanogen iodide. The results obtained with this substance are shown in Fig. 2.

Curve 1 represents the reaction when none of the poison is present. Curves 2 to 11 represent the results with increasing amounts of the poison. When the concentration of the poison is such that a *gram-molecular weight is contained in forty million litres* of the solution, the action of the platinum is very appreciably diminished. The diminution in the velocity of the reaction is increased as the concentration of the poison becomes greater and greater. When the poison has acquired a concentration of a gram-molecular weight in about thirteen million litres, the velocity of the reaction is reduced to one-half.

These curves show that the colloidal solution of platinum can *recover* also from the poisonous action of cyanogen iodide, provided the poison is not too concentrated. If the dilution is greater than a gram-molecular weight in a million litres (curves 2 to 6) the platinum can recover in part from the effect of the poison, as is shown by the curves becoming convex to the abscissa. If the concentration is greater than one million litres the curves remain concave to

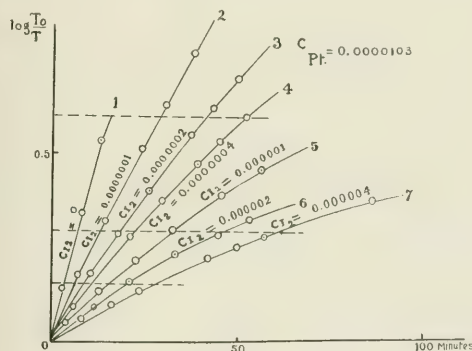


FIG. 3.—IODINE.

the abscissa, which means that the colloidal solution cannot recover from the effect of the poison.

It should be noted that cyanogen iodide is one of the strongest poisons toward blood and protoplasm in general.

The effect of one other poison will be taken up, since it represents the case where the colloidal solution cannot recover at all from the poisonous effects. This poison is *iodine*. The results obtained are shown in Fig. 3. From what has already been said concerning the curves in Figs. 1 and 2, the curves in Fig. 3 are self-explanatory. It will be observed that none of the curves become convex to the abscissa, which means that no matter how dilute the poison, provided that it is sufficiently concentrated to have any appreciable effect, the platinum cannot recover from its influence.

The curves show also that iodine is a powerful poison on the colloidal metal, and it is known to be an intense blood poison.

In a manner exactly analogous to that described above, Bredig and Ikeda have studied the poisonous action of about thirty substances on colloidal solutions of platinum.

The strongest poisons in addition to those described above are mercuric chloride, hydrogen sulphide, sodium thiosulphate, carbon monoxide, phosphorus, phosphene, arsene, mercuric cyanide and carbon bisulphide. From the effect of some of these substances the platinum was able to recover, as in the cases of hydrocyanic acid and cyanogen iodide, while the action of others remained permanent as with iodine. Among the substances which are less poisonous to the platinum are aniline, hydroxylamine, bromine, hydrochloric acid, oxalic acid, hydrazine, and dilute nitric acid increased the activity of the colloidal platinum in breaking down hydrogen dioxide, and ammonium chloride.

The weak poisons are; phosphorous acid, sodium nitrite, nitrous acid, pyrogallol, nitrobenzene, ammonium fluoride, etc.

A few substances were found to be nearly neutral in their action, such as potassium chlorate, ethyl alcohol, amyl alcohol, ether, glycerol, oil of turpentine, and chloroform; while formic acid, hydrazine, and dilute nitric acid increased the activity of the colloidal platinum in breaking down hydrogen dioxide.

At the close of their paper Bredig and Ikeda compared the action of a number of substances on the power of colloidal platinum on the one hand, and of blood on the other, to break down hydrogen dioxide. Their results are given in the following table:

RETARDATION OF THE CATALYTIC DECOMPOSITION OF $H_2O_2$ .		
	BY BLOOD.	BY COLLOIDAL PLATINUM.
Hydrogen Sulphide...	No catalysis.	Catalysis very strongly retarded.
Iodine.....	Catalysis very strongly retarded.	Catalysis very strongly retarded.
Mercuric Chloride....	Catalysis almost entirely prevented.	Catalysis very strongly retarded.
Mercuric Cyanide....	Catalysis very considerably weakened.	Catalysis very strongly retarded.
Hydrocyanic Acid....	Catalysis very considerably weakened.	Catalysis very strongly retarded.
Hydroxylamine.....	Catalysis entirely prevented.	Catalysis strongly retarded.
Amyl Nitrate. ....	Catalysis strongly retarded.	Catalysis strongly retarded.
Nitrobenzene .....	Catalysis appreciably weakened.	Catalysis slightly weakened.
Pyrogallol .....	Catalysis not lessened.	Catalysis slightly lessened.
Arsenious Acid.....	Catalysis inappreciably lessened.	Catalysis slightly lessened.

	BY BLOOD.	BY COLLOIDAL PLATINUM.
Potassium Chlorate...	Catalysis slightly decreased.	Catalysis not decreased.
Aniline .....	Catalysis strongly increased.	Catalysis considerably decreased.

That there is a general agreement between the action of poisons on organic and inorganic ferments is unmistakable from the above results. Certain differences, however, manifest themselves as in the case of aniline, and it is impossible to say at present what these mean.

An impartial examination, however, of all the evidence bearing upon the relation between organic and inorganic ferments will certainly lead to the conclusion that these analogies are not accidental. The state of mind of Bredig on this whole problem can be seen best by quoting the following paragraphs from his monograph on this subject:

"All these facts point to an unmistakable analogy between the contact actions in the inorganic world, and the actions of ferments in the organic world. As in the case of my colloidal catalyzers, we are dealing with reactions in which enormously developed surfaces are involved, so is it probable that the same condition obtains in the actions of ferments, enzymes, blood corpuscles, and oxidizing and catalyzing organic substances. We see, therefore, that the organism develops its enormous surfaces in the tissues and colloidal ferments not only because it requires osmotic processes, but on account of the very great catalytic activity of such surfaces. If, as Boltzmann says, the war for existence which living matter must wage is a war about free energy, certainly, of all the forms of free energy the *free energy of surface* is the most important for the organism.

"In conclusion, I need scarcely state that I do not maintain that there is any mysterious identity between the metals and the enzymes. But without exaggerating the overwhelmingly large number of analogies, we are compelled to regard the colloidal solutions of the metals, in many relations at least, as *inorganic models of the organic enzymes*."

The author would refer the action of the colloidal solutions of the metals, the enzymes, and catalysis generally to the *surface energy* possessed by these substances. We are thus led one step nearer to the solution of the nature of catalysis, which underlies so many of the processes of living as well as dead matter.

## GREEK IN MEDICINE.<sup>1</sup>

BY ACHILLES ROSE, M. D., New York.

The subject which I have the honor to place before you is as important as it is fascinating. Eloquence I have none; fortunately for me no eloquence is required to excite your interest in the cause I am pleading.

The significance of Greek in Medicine can only be appre-

ciated when we know the complete history, or at least certain facts of the complete history, of the Greek language. Our schools give us only a fragment of this history, because our schoolmasters, our college professors, know only a fragment of the Greek language; of its history they know still less.

<sup>1</sup> Read before the Book and Journal Club, Baltimore, Feb. 19, 1902.

The history of ancient Greek literature even is not the history of ancient Greek language, for that part of the ancient Greek literature which has been transmitted to us through the classical writers is an artistic product beginning with Homer and ending with the end of paganism. This artistic product was not the language really spoken.

Ancient Greek language begins with the origin of the Greek race and extends to the present day.

Greek is the oldest of all the living languages of civilized nations. From the classical period of the Attic orators down to the present day it forms an unbroken continuation of classical Attic.

We shall see how Byzantine and Mediæval Greek, or Middle Greek as it is called, thus far have received but little attention; they have, as a rule, not met with any sympathetic interest on the part of the classical students. These phases of the language have on the contrary been branded with unmerited reproach and scorn, and the Greek spoken at the present time is made the object of ridicule and discredit, even by men otherwise of learning, who have no idea of living Greek and who repeat only what they know from hearsay, or what they have read in papers and periodicals written in an inimical spirit towards Greece.

In the middle of the fifteenth century, after the fall of Constantinople, Greek fugitives came to all parts of Europe; and it was they who introduced the study of Greek and laid the foundation of the "Western" school. The first act of this school, still in its infancy, was to do away with the traditional pronunciation and then to declare Greek a dead language.

They cut off all direct connection between the verbal and the written tradition of Greek. At this time the study of philology in regard to Greek became unscientific and has remained so ever since, for the study of a language like the Greek must not confine itself to written tradition. Only the study of the two forms of tradition in connection with each other renders possible a scientific understanding of the old phase as well as of the new; the two forms of tradition influence each other. One of the influences is that of the older monuments of literature upon the later phases of the language, and this influence is the greater the more the old literature is manifold, and the more diligently it is studied by the descendants.

With the close of the 6th century B. C. the dialect of the Athenians, the so-called Attic, prevailed over all other sister dialects, and eventually absorbed them. It was the Attic, because Athens, particularly after the Persian wars, rose to absolute dominion over all other Greek communities, and finally became the metropolis of all Greek races.

There has never existed a language which permitted greater distinction of expression or style than the Attic. To speak and to write Attic was, on account of its richness, as easy as it was difficult to do so with elegance. In speaking of Attic, therefore, we must not infer that all Athenians and Atticized Greeks wrote and spoke the classical Attic portrayed in the classical literature. We have to take into

account, as is shown by force of logic, by historical investigation, by modern analogies and by daily experience, that it is an indisputable fact that no writer uses the same diction, both in writing and in every-day speaking. Every Greek at present, for instance, is at liberty to use the colloquial language or even his own dialect in every-day intercourse; but when he proceeds to commit his thoughts to paper he is compelled to follow the Attic grammar—the style, as a matter of course, varies with the degree of individual education of the writer. The colloquial speech, therefore, is hardly presented in literature. It never attained recognition or favor among the educated writers; on the contrary, there has been at all times a general prejudice against it, and the writers of all times have made it a special point of honor and pride to make the least possible concessions to the popular vocabulary. It is true that, during the Turkish rule, attempts were made to use the vulgar language in literature. Roman Catholic priests, for propagandist purposes among the Greeks, translated the liturgy into the idiom of the people. The Greeks are especially careful not to employ common language when they speak of sacred things. For these, and many more reasons, the Catholic priests did not succeed. To what extent the whole Greek nation is opposed to the idea of introducing popular language into literature, has been demonstrated again quite recently by the events in Athens which took place when the Queen attempted to introduce a translation of the gospel into vulgar Greek. Here, in New York at least, there was a most unanimous expression of horror among my Greek friends in regard to the idea of this translation. Reading the Greek criticisms in the papers of the time when the first specimens of this translation were published I learned how rich the Greek language is in derisive adjectives, for the papers made use of the entire wealth of these adjectives against the translation.

These facts show how unjust it is to draw a parallel between classical Greek, in its artistic as well as its artificial form, and the everyday colloquial Greek of the masses of the present day; but such injustice is the rule, even among philologists.

The final subjection of Greece to the Macedonian rule ended her glorious days. At that time, the conquests of Alexander the Great, in Asia and Egypt, threw the East open to the Greek population. Multitudes of Greeks came to Asia, Egypt, North Africa, Southern Europe. The Greek language, then already Atticized, was triumphant everywhere, became an international language. The great mass of Hellenes, who had come with Alexander the Great, were forced more and more, in order to understand each other, to give up their provincial idioms, and to adopt the Attic dialect. This generalization of the Attic was called the *κοινή*, that is, the general language. Attic became *κοινή*, and this is identical with New Greek. Let us bear this fact in mind, because it is of paramount importance. New Greek originates from the *κοινή*, not from the dialects. Attic *κοινή* has conquered the old dialects. The inscriptions of the time

of Alexander the Great at first were partly in dialect but finally nothing dialectical remained.

There were some writers during the 1st and 2nd centuries of the Christian era, who for love of archaism, tried to write the old dialects; but they found themselves unable to do so, and committed all sorts of errors in their writings. This would have been impossible if the old dialectical forms had still been alive in their old purity, that is, if they had been spoken still.

Then the balance of culture and learning shifted to the East, Alexandria becoming the principal centre of classical education and learning; hence this period is called the Alexandrian.

The Greek population had settled abroad among alien races as soldiers, colonists, tradesmen and the like, and formed only a minority among the natives and a sort of colonial—the Levantine—Greek developed, but whatever foreign elements had been introduced at that time were eliminated again in subsequent periods.

During the Græco-Roman period (150 B. C. to 300 A. D.) the Romans, instead of Romanizing their Greek subjects were Hellenized by them. Whatever Latin words, referring to Roman associations and novelties had been adopted in a more or less Hellenic form during this period, were also eliminated again.

While thus the language was in danger of adopting foreign elements, in danger of comparing unfavorably with the Attic of the glorious olden times, many scholars at that time, and later on the great majority of their successors, endeavored to check the progress of this "common" tongue, as they called it, that is, the unclassical Greek, and to revive the pure Attic. They were called the Atticists or Purists. The extreme Atticists thought one should not only imitate the old genius, the right composition of speech, the pure and simple diction of the ancients, as was the teaching, for example, of Dionysios of Halicarnassos, but also to copy scrupulously the words and forms.

The literature of the extreme Atticists or at least the writings of these Atticists gives no picture of the language of their time.

The writers of the Graeco-Roman period were 1. Atticists; 2. Conventional writers who wrote Attic with many concessions to the spirit of the time; 3. The Levantine Group, represented by the Asiatic Greeks and Hellenized foreigners. The New Testament is written in Levantine Greek.

Christianity originated in Asia Minor, which was ruled by Rome but spoke Greek. Christianity sprang up in the midst of the masses, borrowed from Hellenism its language, and became a part of the Hellenic race and nature. The very founder of Christianity (presumably) and his apostles (certainly) preached and wrote in Greek. Nothing has been more potent in the preservation of the old Greek than the influence of the Church.

When the Roman Empire was dying out it had the good fortune to be absorbed in the life of Greece and it derived from that union a renewed energy which secured for it

another millenium of existence in the Byzantine Empire. The first Byzantine emperor, Constantine the Great, adopted the Christian faith and was the first Christian emperor.

Until recently the Byzantine era was the least known and the most obscure in the field of historical study, the history of the Byzantines, of their Greek and Christian state over a thousand years of existence, was treated with great injustice, exaggerated severity, and contempt. Two writers especially, Montesquieu and Gibbon, have done a great deal to promulgate error and injustice in regard to Byzantine history. There exists even at this present day no fair history of the Byzantines in the English language. What applies to Byzantine history applies likewise to Byzantine literature and language. The only collections of importance from this literature were made in France during the 17th century under the auspices of Louis XIV, in the *Corpus Historiæ Byzantinæ*, a work of 42 very large volumes in folio; and now the works of the Byzantine medical writers are collected and published under the editorship of Foustanos, the editor of the Greek Medical journal *Ἱατρικὴ Πρόοδος* of Syra.

Philologists are accustomed to distinguish ancient Greek from modern Greek without considering middle Greek, notwithstanding the fact that there is nothing in modern Greek which has not come from ancient Greek by way of middle Greek. The study of this latter phase of the language furnishes the best information for the scientific knowledge of modern as well as of ancient Greek.

Ten years ago there appeared in the German language a work, modestly called "Einleitung in die neugriechische Grammatik," by G. N. Hatzidakis, a Cretan, Professor of Philology at the University of Athens, and this book gives more valuable instruction on the history of Greek than all the other books, written on this subject, together.

A great number of forms, words, and constructions, which, according to the literature of several ages, one would believe to be lost, can be found to-day in the different dialects spoken in different parts of Greece. Phenomena which would appear to be modern can be shown through these dialects to have originated in the oldest times; indeed many old phenomena have been preserved to this day in the dialects, although the literature of the middle ages and of modern times bear no witness to them. In view of these facts, we can readily see that only a man like Hatzidakis, a philologist, a native Greek, who can identify himself with the Greek peoples' dialects is qualified to give the history of Greek.

During the Mediæval period (from 1000 to 1450) in Greece proper, a vocabulary of the feudal reign of the Franks, chiefly bearing on chivalry and gallantry was mixed with Greek, but never struck root in the Greek language. All these foreign words soon passed into oblivion. Similar considerations apply to the succeeding dominion of the Venetians, whose institutions never became popular in Greece.

A striking illustration of the failure which attended the efforts of Venice—the most civilized and mighty of all foreign rulers in Greece—to assimilate her Greek subjects, may be found in the present state of Crete. This island remained

under the Venetian dominion, and formed a dependency of powerful organization for an unbroken series of more than 450 years (1210 to 1669), yet with all that, hardly any native Cretan Roman Catholic is to be found on the island, and the Cretan vocabulary of to-day does not preserve fifty words which can be traced directly back to the Venetian domination.

It is hardly necessary to speak at this present time of the witty arguments of Fallmerayer; they have no foundation, and have been discredited long ago by all serious investigators. The fact is that, except a very few names of hills and rivulets, there exists not a single Slav word in the Greek language spoken and written to-day.

The Greek of to-day as taught in the schools throughout Greece, the official language of the government of Greece is pure Attic Greek, as pure as it ever was. It is the immortal Greek in all its youth and beauty, free from foreign elements.

Our Græco-Latin onomatology is evidence that our science originated in Græco-Roman antiquity and these classical languages in our onomatothesia have given our science an international character and established a union of the different peoples for the good of science.

Our Western civilization has adopted from the Greek literature the really moving thoughts and the facile forms. The school of Athens formed the background of all learned activity. Homer, Aristotle and Plato have continued to be, up to our time, the teachers of mankind. The classical writers of Rome were in their works a long way behind the Greek authors; indeed, the best among them are indebted to their Greek antecedents for their education. The Latin language was the first one which borrowed from the Greek, and the languages of all civilized nations, above all the German, French and English, have done likewise. The number of Latin medical terms is inferior to the number of words from the Greek, and medical writers, when they coin new words, prefer to borrow from the Greek.

Greek has been the international language of the world, and Virchow, in his inaugural address as rector of the University of Berlin, said that it was from the beginning a weak side of the humanistic educational institutions to favor Latin as the international language of scholars.

But we will not dwell to-night on Latin, nor shall I speak of Greek as the international language for scholars. I shall confine myself to speaking of Greek in medicine, and to this end I may be permitted to say first a few words on our onomatology in general.

Twenty years ago, in an article which appeared in the Berliner Klinische Wochenschrift, Virchow said: "Is it not justifiable at the present time to remind the physicians that they should use all possible exertion to show their scientific training in all, even in apparently small things? Is it not the first characteristic of a man of science that he should understand how to employ the language of science? The first thing by which the expert demonstrates his qualification is the correct use of technical terms; this specially

causes respect for him, and nothing more enhances his utility"; and he closes his remarks with the wish that his views might be generally adopted.

If we address this admonition to the medical profession at large we shall have to say: Would it not be justifiable at the present time to remind the profession to prove our science by establishing a scientific onomatology?

The incorrectness of many of our medical terms cannot be denied, but the extent of this incorrectness is larger than most of us have ever conceived; the evil is increasing every day, and the remedies thus far suggested have only brought confusion; they are not, and have not been, taken seriously; they have only brought discredit.

Hyrtil, who was without doubt the best classical scholar among the medical men of his time, gave us a work entitled *Onomatologia Anatomica*, in which he exposed a great number of terms as being incorrect, ridiculous, absurd, and, hence, unscientific; but he says quite modestly: "The idea of reforming the anatomical language could not enter my mind. To this end is required a committee of anatomists, selected *ad hoc*, who are at the same time linguists, and as coöperators, philologists, an *Accademia della Crusca Anatomica*. I merely had the intention of demonstrating to those who will take the pains to read this book the necessity of reform."

It may appear audacious and impious on my part when I say: with all his classical training, Hyrtil himself added errors, because in one requirement he was wanting, like the rest of the would-be reformers, he had no idea of living Greek, for he quotes colloquial or vulgar Greek and calls it New Greek.

Henle, an anatomist of the same high rank as Hyrtil, attempted to simplify the anatomical onomatothesia, but only added a new complication, because his suggestions were not uniformly accepted; he likewise did not consider the existence of living Greek.

Virchow, in his inaugural address on Greek in medicine, had in view only Greek as taught in our schools; living Greek he did not mention. All the lexicographers outside of Greece have been obliged to ignore it, because the medical word-makers of our times have ignored it, or have quoted vulgar Greek, which our Greek colleagues exclude from scientific literature, or, worst of all, they have introduced words which they stigmatized as "New Greek" which are not Greek at all.

It is not necessary to enumerate all the vain attempts at reformations of our onomatology; a single one, and I select the one which is most conspicuous at present, will suffice. We shall see why they were all of no avail, but we shall also see how we really can secure scientific onomatology which will stand as long as our science is taught, and which will be beyond all criticism. But let us first speak of the nomenclature of the German Anatomical Society.

The German Anatomical Society appointed a committee and raised the necessary funds, about three thousand dollars, from contributions by different medical academies to furnish an onomatology with all names in grammatically correct

Latin. *All Names in Latin!* The members of the committee were all prominent German anatomists and all thorough classical scholars; they worked hard for seven years; thus they conducted an immense amount of correspondence and had many meetings in Munich, Vienna, Goettingen, Strasburg and Basel; their sessions in Munich, for instance, commenced at 8 A. M. and lasted until 6 P. M., in Vienna even until late into the night. In the year 1895 the new anatomical nomenclature—*Nomina Anatomica*—as the title is, was published, and whoever chooses may accept the names of this onomatopoesia. Most of these names are by no means Latin, but Latinized Greek, or they are unscientific hybrids. In some of them of more than two syllables we find the syllables alternately taken from one and the other language.

The German Anatomical Society has undertaken a thing which is an impossibility—namely, to restore to life, to develop further, a dead language.

Had the society, however, taken the living Greek for a basis instead of the dead Latin, had they consulted real Greeks, the professors of anatomy of the University of Athens, they could have fulfilled their promises, executed all their intentions without the arduous labor of seven years.

The result of the labors of the German Anatomical Society demonstrates that even an academia, as suggested by Hyrtl, will not succeed so long as it applies dead language to new conceptions, and treats a living language as it were a dead one.

As mentioned before, the classical languages in our onomatology give our science an international character and continue to establish and secure more and more a union of the different nations for the good of science. But science requires that our onomatology should be correct and scientific, and this it can only be when new conceptions are named in Greek; and no new formation in Greek can be proven correct that does not meet with approval of our Greek colleagues.

There exist words in our everyday language which a Greek friend of mine is in the habit of calling *ελληνισμους*, that is "Greek seeming or supposed Greek," as for instance the word bicycle or telegram; they are an impossibility in Greek and such *ελληνισμους* words we have in great number in our onomatology. Most of them are simply horrid, notwithstanding that they were coined by men of great learning, by profound classical scholars. Every one of us has had ample opportunity to observe how awkwardly English is spoken and written by those who have learned the language in some German or French schools by means of grammar and lexicon only, and this awkwardness is manifested by our medical word-makers who coin what they suppose to be Greek terms without being familiar with esoteric Greek, as only those who are Greeks or who have lived among them can be. Now let us see how the Greeks go to work when new formations are required: When Greece had regained her liberty after almost four centuries of Turkish bondage, a regular government was to be erected. Countless numbers

of demands were made on the language. A new life, a culture of which there had been no idea before, appeared suddenly before the Greeks. The language had to keep pace with the many new political, scientific, technical, commercial, journalistic requirements. Another nation would certainly, under such circumstances, simply have adopted with the foreign ideas the words also of foreign people, and would have formed a hybrid language. Not so with the Greeks. Their history, their national pride led them to exclude foreign words, led them to take the necessary elements from the old Greek to create new symbols for new ideas. Constructions and forms were remodelled after the old Greek, incorrect elements, when discovered, were extirpated with more and more severity and tact, and so it is to-day. Before a new formation is introduced into the regular language it has to stand a severe test and criticism. Nothing will be accepted and introduced into the regular language which deviates in any way from the genius of the Attic language. We need not, therefore, fear that terms which we might accept from our Greek colleagues would be contrary to the spirit and the form of classical Attic.

The facts I have presented to the Book and Journal Club of the Medical and Chirurgical Faculty of Maryland will, I am certain, find an echo in the medical profession. There exists a well-pronounced demand by all true men of science for purity and correctness of medical language. Professor R. Kossmann, of the University of Berlin, whose name as a gynecologist is familiar to you, but who is not only a gynecologist, but has also distinguished himself as a philologist, says: "In forming our pathological and surgical technical terms we can by no means dispense with Greek, and so long as we admit that the retention and introduction of Greek synonyms for pathological and surgical expressions is a necessity, we have for the sake of correctness and beauty of language to decide to go a step further, to do away with hybrid terms and establish pure Greek synonyms in their place. Whoever has familiarized himself with classical literature will find it more and more intolerable to name a scientific conception by a Greek- or Latin-like sounding word monstrosity, especially when he knows the real Greek name."

Dr. H. Zimmerer, a distinguished professor of philology in Germany, one of the exceptions among the German philologists in so far that living Greek is familiar to him, honored me by the invitation to cooperate in a new edition of a medical lexicon. In my turn I secured the assistance of a Greek friend, Basilios Leonardos, doctor of medicine and philology, director of the Museum of Inscriptions of Athens. I thus learned that professors of the University of Athens would be ready to aid in case a thorough revision of our onomatology in regard to Greek should be intended.

I shall congratulate myself if I have succeeded in demonstrating the possibility of a scientific onomatology and displayed the significance of Greek in Medicine in a new light.

## ON SYPHILITIC DISEASE OF THE CEREBRAL ARTERIES.

By F. C. GOLDSBOROUGH.

*(From the Pathological Laboratory of the Johns Hopkins University and Hospital.)*

The literature on the subject of the vascular changes in syphilis has been so frequently and so well reviewed that it need be merely briefly summarized here. More detailed references may be found in the papers of Abramow,<sup>1</sup> E. Meyer<sup>2</sup> and Oppenheim.<sup>3</sup>

Heubner<sup>4</sup> first accurately described these changes as specific in their characters and easily distinguishable from the ordinary arteriosclerotic processes. The specific nature of the changes has been doubted by many authors, but seems now to be pretty generally accepted. The definitely circumscribed thickenings of the wall leading often to obliteration of the vessel, the almost acute course, and the occurrence in young people often without general arterial affection, characterize the syphilitic changes fairly well. Instead of a degenerative lesion in the wall which leads to a diffuse widening of the vessel often with calcification, we have a nodular thickening which is definitely gummatous in its histological characters which narrows the vessel and in its late stages may undergo a caseous degeneration.

As to the point of origin of this gumma formation opinions differ widely. Heubner considered the thickening as primarily due to a proliferation of the endothelial cells with the formation of a mass of spindle cells and later affection of the outer coats of the artery.

Baumgarten<sup>5</sup> agreed with Heubner as to the specific nature of the process, but concluded that the changes began in the adventitial coat. There when they constituted a distinctly gummatous formation they could be recognized as syphilitic, while the much less advanced alterations in the corresponding intima were as yet not particularly specific in character. Köster<sup>6</sup> went even further in denying the occurrence of any proliferation of the endothelium. Recently Junzo Nagano<sup>7</sup> clearly states his conclusions which in general agree with those of Baumgarten, as follows: "In the first place only the adventitia is constantly diseased—where the intima is affected the adventitia is always involved, but the reverse is not true. I do not hesitate therefore to consider the adventitial change the primary and essential, while the changes in the intima are secondary. While the intima is greatly thickened in some places, still in many this change is quite lacking. The media, on account of its very slight alteration, does not enter into consideration as a point of origin for the process."

As to the part played by the media, Rumpf<sup>8</sup> put forward the idea that the syphilitic process originated from the capillary system of that layer and thence extended to the adventitia or to the intima. Finally Oppenheim declared that the three coats of the artery may become diseased independently of one another.

Thus we find these authors expressing every possible opinion as to the point of origin of this syphilitic new formation in the vessel wall. Certainly in advanced cases all of the walls are found involved, and evidence as to this point can only be expected from examination of the early stages in the process or possibly examination of the advancing margins of the diseased portions of the vessels.

The following case occurred recently at the Johns Hopkins Hospital:

Mary D., colored, aged 30 years, admitted March 22nd, 1901, complaining of headache. There was no history of gonorrhea or lues. She had had rheumatism 2 years ago lasting over 5 months. Had given birth to two children, one 10 years ago and one 9 years ago; the first was still-born, the second died, aged one and a-half years.

She complained of having had headache for more than a year and five months; at the onset there were several attacks of fainting lasting through a week at a time. Recently her eyes had failed and she had become stupid and slow mentally. There were no convulsions.

On admission there was a bulging of left eye; no paralysis, although there was some weakening of the muscles of the right side of face and of left arm. Reflexes were normal.

Physical examination of the abdominal and thoracic viscera negative. The blood count at this time showed:

Hæmoglobin .....	40%
R. B. C. ....	2,700,000
Leucocytes .....	8,000

On April 22nd definite optic atrophy developed. On April 29th lumbar puncture was performed with no results. On May 10th there was ptosis of the right lid; reflexes became exaggerated; there was stiffness of the legs, arms and neck. May 30th patient went into coma and died June 2nd.

Urine showed traces of albumin, but no casts.

Autopsy was performed June 2nd.

The viscera in general showed no abnormality except for the presence of small caseous masses in the liver, which were surrounded by widely radiating scars; in other portions of the liver such scars occurred alone.

In exposing the brain and cord, the vessels of the pia over the surface of the brain were found to be much injected and

<sup>1</sup> Abramow, *Ziegler's Beiträge zur Path. Anat.*, 1899, Bd. 26, S. 202.

<sup>2</sup> E. Meyer, *Centrabl. f. Allg. Path. u. Path. Anat.*, 1898, Bd. IX.

<sup>3</sup> Oppenheim, *Handb. d. Specielle Path. u. Therap.*, herausg. v. Nothnagel, 1896, Bd. IX.

<sup>4</sup> Heubner, *Dieluetische Erkrankung der Hirnarterien*, Leipzig, 1879.

<sup>5</sup> Baumgarten, *Virchow's Archiv*, 1878, Bd. LXXIII, S. 90.

<sup>6</sup> Köster, *Berliner Kl. Wochenschr.*, 1876, Nr. 31.

<sup>7</sup> Junzo Nagano, *Virchow's Archiv*, 1901, Bd. CLXIV, S. 355

<sup>8</sup> Rumpf, *Die syphilitische Erkrankung des Nervensystems*, Wiesbaden, 1887.

there were here and there minute hæmorrhages; these were also found on the under surface of the frontal lobe. There was a marked opacity of the pia along many sulci, especially in the frontal region and longitudinal fissure; this was also marked in the fissure of Sylvius. Many of the arteries in this region showed minute greyish nodules scattered along their course. This condition was especially marked on the basilar portion of the brain where, over the optic chiasm, there was an opaque mass forming a thick envelope which involved also the carotid artery; each of the cranial nerves was developed separately in such an opaque mass.

Over the pons and between the cerebellum and cerebrum there were similar irregular yellowish masses which in the peripheral portion were sometimes translucent. These formed at the junction of the vertebral arteries a mass measuring 1.5 cm. in diameter.

Over the dorsal surface of the cerebellum the beading of the arteries was especially well seen. The cerebral ventricles contained no excess of fluid and the ependymal surfaces were smooth.

On section the brain substance appeared normal throughout.

*Microscopical Examination.*—Sections of several parts showed that the brain was practically normal, although here and there an increase in the number of periganglionic cells was observed. The lymph-sheaths of the small vessels were filled with deeply stained small mononuclear cells. Minute hæmorrhages were also to be seen about some of the smaller vessels. Some of these vessels showed a hyaline degeneration of their wall which was somewhat thickened, homogeneous in appearance and without nuclei.

Sections were made through the thickened portion of the meninges in various places, and also so as to include the nodular thickenings of the vessels. The smallest of these were preserved for investigation and sections, both transversely and longitudinally, were made.

The meninges in the neighborhood of the affected vessels proved to be somewhat thickened, and for the most part infiltrated with cells; the greater number were deeply stained, small mononuclear cells with very scant cytoplasm; polynuclear cells, however, occurred here and there.

In a cross section of one of the small thickened vessels the lumen was found to be disproportionately small, but filled with blood and lined with intact but somewhat thickened endothelium. Outside of this there was found a mass of epithelioid cells in a dense reticulum. These cells were variable in size and their form was sometimes much elongated. This tissue was somewhat eccentrically arranged so that on one side of the lumen it formed a thick mass where the cells became less numerous and the intercellular substance increased; here much nuclear distortion and fragmentation occurred; there was, however, no actual caseation. The whole mass was surrounded by the much thickened elastic lamella which was very tortuous on the side near the lumen, but stretched out smooth over the thickened mass on the other side.

The media was intact over the part of the vessels where the thickening was least; the rest of the media was stretched out thin and its laminae were spread apart by the invading cells which were themselves undergoing fragmentation. The nuclei were much misshapen and were apparently disintegrating.

In the adventitia the tissue changes were especially marked. There there was great proliferation of the spindle-shaped connective tissue cells or epithelioid cells which made up the bulk of a considerable mass of tissue. Among these were seen many small round cells. Giant cells were infrequent, but occurred sometimes. They were more often seen just inside the elastic lamella. Very characteristic, however, was the great distortion of the nuclei of the epithelioid cells in areas in the nodule surrounding the patches of caseation which pretty regularly appear after the nodule had reached a certain size. The extension of such a caseated area toward the media led to the peculiar disintegration observed in the stretched-out portion of that layer.

In several longitudinal sections of such a vessel the relations are even clearer. The spindle cells of the subendothelial tissue are arranged almost entirely longitudinally, so that that tissue appears like a well-defined fibrous tissue. This thickening of the intima seems to correspond generally with the areas of thickening of the adventitia, but it is important to note that practically always the adventitial changes were obviously more advanced than those of the intima, and it was there that caseation first appeared in each case.

The condition was practically the same except in degree in all the vessels examined. The only change in some of the very small ones was a diffuse infiltration of the adventitia with lymphoid cells.

In some places more than one endothelium-lined lumen was seen within the tissue inside the elastic lamella. In the explanation of this phenomenon, Rumpf's idea that widened newly formed vessels in the tissue which goes to obliterate the original lumen give rise to these channels, seems more plausible than their interpretation as parts of the original lumen which have been partitioned off. There seemed to be a new formation of muscle about the endothelium of these secondarily formed blood channels. The membrana elastica in the affected vessels is generally enormously thickened, but no definite splitting or reproduction of the membrane has been observed.

Certain portions of the central nervous system itself were involved in these processes; the optic tract, for example, showed on section a dense infiltration with small round cells which infiltrated along the septa dividing the bundles of nerve fibres. The infiltrating mass was found to be continuous with that surrounding the carotid artery, although the carotid artery internally showed only the changes ordinarily seen in arteriosclerosis.

Also in the pons underlying the caseous masses about the basilar artery, there was a deep involvement of the nervous tissue which was much infiltrated and degenerated.

The ventral root of the 3rd cervical nerve was also extensively infiltrated with new tissue elements which pushed aside the nerve fibres and tended to destroy them. Some portions of this mass had even undergone caseation. A great many sections were stained for tubercle bacilli, but always with negative results.

From all this it is evident that we have in this case pre-eminently an affection of the vessels, the meninges and central nervous substance being relatively little involved. The lesions consist in thickening in the walls of the vessels which are histologically gummata with the characters recognized in

gummata elsewhere. These gummatous lesions are most advanced in the adventitia, being generally accompanied by proliferation of the intima in a corresponding locality. The process, therefore, probably begins in the adventitia. It is, on account of its characteristic histological appearance, quite as specific in its nature as the tuberculous change in the vessels in tuberculous meningitis and is not to be confused with the ordinary arteriosclerosis.

In closing, I wish to express my appreciation and thanks to Dr. W. G. MacCallum, under whose supervision this work was done, for his very kind assistance and advice.

## PARA-COLON BACILLUS.<sup>1</sup>

By RICHARD P. STRONG, M. D., U. S. A.

A single case of infection with para-colon bacillus has come to us. This case was not seen during life, but the body was sent from Santa Cruz to Manila, where we observed it at necropsy. The following brief clinical history was obtained later from his hospital record at Santa Cruz:

"On July 5th, 1900, the soldier developed temperature. There were rectal discharges of blood and mucus. The chart shows the course of the fever to the time of death, July 31st. No departure from the ordinary type of typhoid fever."

The necropsy was held forty-two hours post mortem. The body was extremely emaciated; there was considerable post mortem change and gas in the sub-cutaneous tissues. The heart muscle was pale and yellow in color. The valves were all normal. The arch of the aorta and coronary arteries smooth. The lungs were also normal. The mesenteric lymphatics were swollen and some, along the small intestine, hemorrhagic. The spleen was very large and soft, and the pulp somewhat dark and considerably increased in amount. The liver showed advanced fatty degeneration. The capsules of the kidneys were not adherent; the organs were pale and yellow in color. Both the large and the small intestine were normal throughout, except for a moderate catarrh and a few superficial hemorrhages. The solitary and agminated follicles showed no lesions. The other organs were normal. Stained cover-slips from the liver showed a large capsulated bacillus, which, as it did not appear in aerobic cultures from the spleen, we regarded as probably bacillus aerogenes capsulatus; the cover-slips also showed smaller bacilli. Fresh smears from the spleen showed a few crescentic æstivo-autumnal malarial parasites, and a fair amount of malarial pigment. No hyaline bodies could be found.

As we desired a fresh typhoid culture, an extra number of cultures (four plates) was made from the spleen. After

twenty-four hours a good number of colonies developed on these plates, which seemed similar to one another and resembled colonies of bacillus typhosus or delicate colon colonies. A number of these colonies were planted on all media with the following results:

On agar slants there was a moderately heavy growth; bouillon was at first clouded, after a time a sediment formed at the bottom and often a pellicle on top; hanging drop showed a motile bacillus; stained cover-slips decolorized by Gram; in glucose agar there was a moderate gas production; in lactose agar there was no gas production; saccharose was moderately fermented; litmus milk was at first reddened after fourteen to twenty-four hours, and then turned blue after about forty-eight hours; in Smith's sugar-free bouillon there was no indol production.

This organism was pathogenic for mice in doses of  $\frac{1}{2}$  cc. The same bacillus was recovered from their blood and organs after death. Unfortunately no serum with the patient's blood was tried with the organism recovered.

As is well known, in 1897, Widal obtained from an abscess in the neck, about the œsophagus, after an attack of supposedly typhoid fever, an organism to which he gave the name para-colon bacillus. In the same group with this organism he placed bacillus psittacosis of Nocard and a bacillus of calf septicæmia of Thommasen. Widal's organism presented a strong agglutination for the blood of the patient from which it came.

In 1898, Gwyn reported a case of infection with the para-colon bacillus in a patient with all the clinical symptoms of typhoid fever. He isolated the organism from his patient's blood, whose serum agglutinated this organism, but not the bacillus typhosus. The organism differed in its cultural peculiarities from Widal's organism only in that it fermented saccharose.

Cushing has quite recently reported a third case of para-colon infection, the organism being obtained from an abscess of the rib following an attack of prolonged fever resembling

<sup>1</sup>From Report to Surgeon General "On Prevalent Diseases among troops in the Philippines." (Manila, P. I., Jan. 10, 1901.)

typhoid. The serum in his case also agglutinated the organism he isolated. Cushing worked with Gwyn's bacillus and concluded that neither his own nor that of Gwyn is capable of fermenting any other pure sugar than glucose. Our organism at present is still growing in the laboratory and a culture of it will be sent to you with this report.

In litmus milk with the organism, the change to the red color may be noticed in about fourteen hours; after about forty-eight hours the tube returns to about an equal shade to the control tube, or at the top it may be a little bluer. The bluing gradually continues at the top, while the litmus solution becomes gradually reduced and decolorized at the bottom. Cushing has stated that it can be readily understood if these organisms occupy, at one time or another, the alimentary tract during the course of fever associated with intestinal lesions, they might easily find their way into the portal circulation and cause a superimposed infection on the original disease. He also remarks, however, that the colon bacillus is rarely found beyond the limits of the abdominal cavity, while Gwyn's bacillus and his own were isolated, one from the peripheral circulation and the other from a surface lesion; also both gave an agglutination for the para-colon bacillus and not for the bacillus typhosus. Therefore he is inclined to believe that they were the spe-

cific cause of the disease which resembled, clinically, typhoid fever.

Unfortunately, we were not able with our case to throw much light on the subject, for no serum reaction was tried with the organism and the patient's blood from which it came. So, whether the organism was a post-mortem invader (as Reed has shown the bacillus icteroides, another member of the hog cholera group sometimes to be) or not, we cannot say definitely. At any rate, macroscopically, there were no definite lesions of the intestine to serve as the portal of entry for this organism if it did invade during life. However, no other cause for the death of the patient could be found. It is evident that he was suffering from some infection, as his temperature chart shows, and the few crescents and small amount of malarial pigment would not explain his death from malaria; besides, he had been treated with quinine.

We regret that this case is not complete, but trust that it will be remembered that the necropsy was an outside one, coming from a distance, that the body was already considerably decomposed, that we had heard only accidentally of its being a case of typhoid fever, and were anxious to obtain a fresh culture. For these reasons, also, no tissues were saved from the necropsy. However, it has been thought worth while to mention the case.

## A CASE OF MULTIPLE PRIMARY ADENOCARCINOMA OF THE LIVER WITH CIRRHOSIS.

BY CATHERINE H. TRAVIS.

(From the Pathological Laboratory of the Johns Hopkins University and Hospital.)

Primary new growths in the liver have been the subject of a great deal of discussion in recent times. The literature has been collected by v. Heukelom,<sup>1</sup> and recently by Eggel.<sup>2</sup> The histogenesis of such tumors is made fairly clear by v. Heukelom.<sup>1</sup> Their relation to compensatory hypertrophy and to adenoma is discussed by Orth<sup>3</sup> and by Schmieden.<sup>4</sup> The coexistence of cirrhosis is also considered by these writers, but their conclusions agree very badly.

Although several kinds of malignant growth are described, one definite type stands out, in which are seen nodular tumor formations of atypical cells, an invasion of the vessels, metastases and cirrhosis.

A case of this type was put into my hands by Dr. Wm. G. MacCallum, whose kindly interest in the study and whose assistance I here gratefully acknowledge. I shall endeavor to give a description of the new growth and to discuss its histogenesis and relation to cirrhosis.

The case is that of T. S., a colored man, aged 40. With the exception of the ordinary diseases of childhood and an attack

of influenza, this man enjoyed sound health up to the time of his last illness. He was, according to his own statement, free from venereal taint, and used alcoholics "only as a medicine."

In July, 1900, he began to have attacks of nausea lasting for several days. From this time he was troubled more or less by digestive disturbances. At Christmas occurred a sharp pain in the region of the liver, subsiding into a dull, constant ache. The patient was not aware that he had ever been jaundiced.

On admission to the Johns Hopkins Hospital on February 5th, 1901, he was found to have a much enlarged liver which presented several nodular protuberances along its lower border. The lower part of the right intercostal region showed some bulging. The percussion note was impaired and the breath sounds suppressed over various parts of the lungs. There was no oedema of feet and legs.

The diagnosis of carcinoma of the liver was made.

On March 3rd he was discharged unimproved. On April 4th he was seen at his home and found to have a marked ascites. Paracentesis being performed, four or five litres of fluid resembling pure blood were withdrawn from the peritoneal cavity. He rested well the next night, but died the following day.

An autopsy was performed 26 hours after death.

The body was rather emaciated and the abdomen somewhat distended. In the peritoneal cavity about a litre and a-half of blood-stained fluid was found, and there were blood clots in the pelvis.

<sup>1</sup> Ziegler's Beiträge, XVI, S. 341.

<sup>2</sup> Ziegler's Beiträge.

<sup>3</sup> Pathologische Anatomie, 1887, S. 955.

<sup>4</sup> Virchow's Archiv, Bd. 159, 1900.

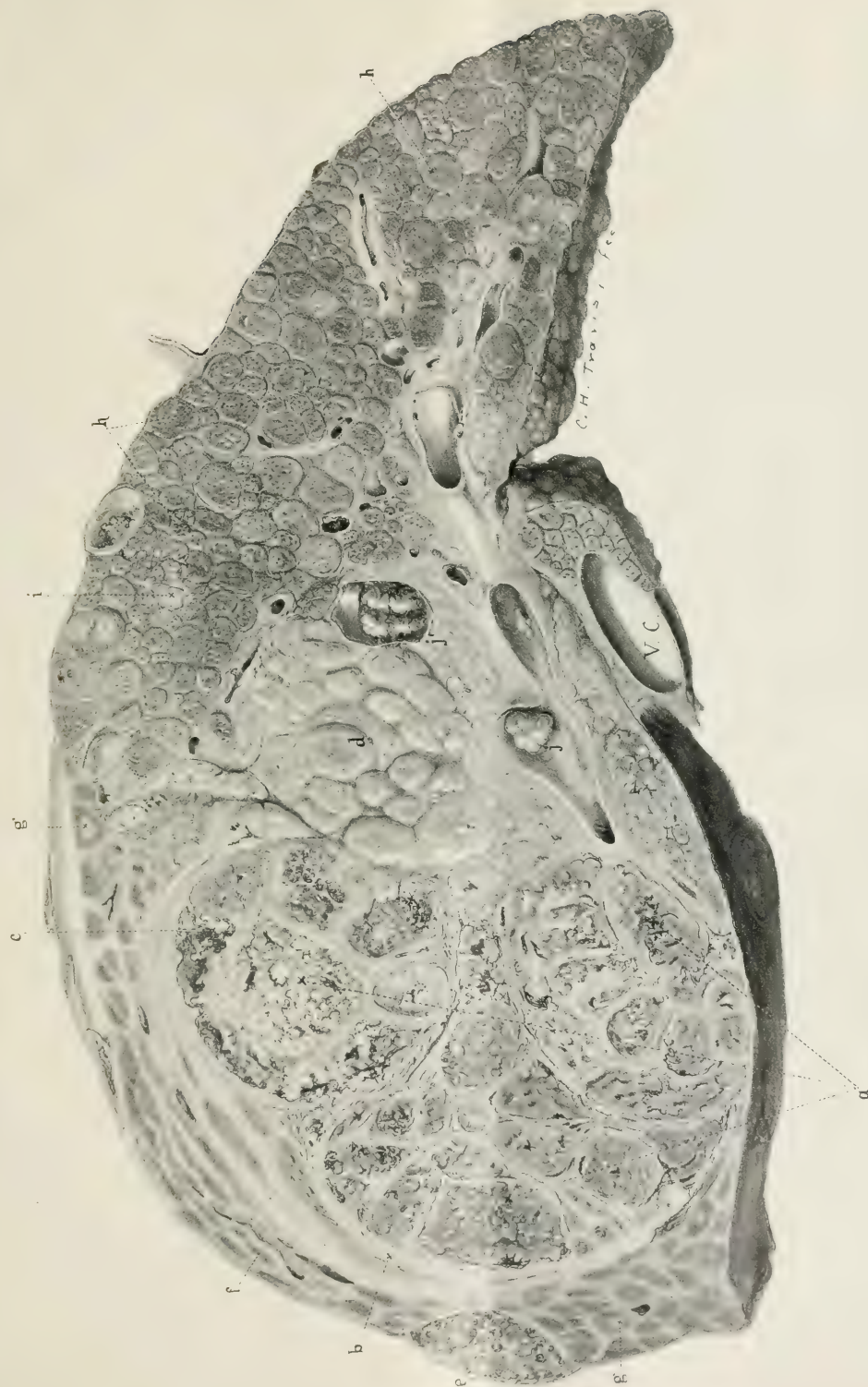


FIG. 1.—Section of liver, natural size  
*a*, Large tumor nodule, broken down at *c*.  
*b*, Fibrous tissue capsule. *d*, Fresh well-preserved nodule.  
*e*, Necrotic tumor mass. *f*, Hemorrhagic liver parenchyma surrounded by connective tissue bands.  
*g, h*, Small tumor nodules. *h*, Areas of necrotic liver tissue in connective tissue frame-work.  
*i, j*, Tumor masses in velus. *v. c.*, Inferior vena cava.



On opening the thoracic cavity, small, opaque, yellowish nodules were seen projecting beneath the pleurae. The largest of these was 10 mm. in diameter. On section they were seen to be rounded masses of a pasty material. The main artery of the left lung contained masses and strands of the same material, and this extended into the arteries all through the lung, and was in some cases traced to the superficial nodules. The lung substance was very oedematous. No further metastases were found in the body.

The liver was enlarged and weighed 3580 grammes. Old adhesions bound the organ to neighboring structures.

The capsule was thickened and the parenchyma soft in consistency. The surface was mottled dark green and yellow, contrasting with the greyish pink ground substance. There were numerous elevated yellow nodules, some 4 cm. or more in diameter, under the capsule, and several large globular masses, quite soft and fluctuant, projected from the upper surface. A similar large mass extended into the peritoneal cavity to the right of the gall-bladder. The superficial portion of this was broken down into a pasty necrotic mass, to which a blood clot was adherent. This was evidently the source of the peritoneal hæmorrhage. The inferior vena cava, on being opened, showed projecting into its lumen from the mouths of the hepatic veins masses of yellowish friable material. The largest of these reached quite to the heart. Section of the portal vein at its entrance into the liver showed it to be similarly filled with a tumor mass.

On section the liver presented a remarkably variegated appearance. The greater part of the right lobe was occupied by a large spherical tumor measuring 16 cm. in diameter. (Cf. Fig. 1 a.) Bounding this on the right was a capsule of tough translucent fibrous tissue. (b.) Trabeculae of the same tissue ran through the substance of the mass, forming a coarse network in whose meshes lay a necrotic, sometimes ragged, material stained green with bile, or hæmorrhagic, or of a pinkish yellow color. To the left of this was a mass of firm, well-preserved, yellowish tumor tissue, also subdivided into nodules. The isolating fibrous tissue bands were here very fine. (Cf. Fig. 1 d.) This mass was seen at one point to be continuous with a portion of the tumor filling a large vein. Round about this large globular mass several smaller nodules were found, some measuring 3 or 4 cm. across. These were at times well-preserved, and again broken down and necrotic. (Cf. Fig. 1 e.) The peripheral portion of the right lobe surrounding these tumor masses was much firmer, consisting of a network of connective tissue trabeculae in whose meshes lay a deep red rather soft material. Small greyish dots were frequently seen in this dark red substance. (Cf. Fig. 1 g.) The strands of fibrous tissue sometimes spread out into large areas, measuring at times 1 cm. across, in which lay opaque yellow dots. The presence of these connective tissue trabeculae gave rise to the nodular appearance on the surface of the liver.

In the left lobe there were no large tumor masses. On section the cut surface showed the same nodular appearance as the outer surface, and seemed to be made up of numerous independent rounded tissue masses, held together by a framework of connective tissue. These rounded areas were partly olive green (cf. Fig. 1 h), partly of a yellowish fawn color (i), and partly hæmorrhagic and more opaque. The green and yellow nodules gave a peculiar marbled mottling to the outer and cut surface of the liver. Some areas were necrotic, soft and pasty, resembling those in the right lobe, except that they were smaller and fresher. Veins occurring in the cut surface were almost constantly filled with the soft, granular, yellow mass of the tumor. (Fig. 1, j, j'.)

The following anatomical diagnosis was made. Primary adeno-carcinoma of the liver with invasion of the portal and

hepatic veins. Metastatic growths in the pulmonary arteries and lungs. Cirrhosis of the liver. Ascites. Hæmoperitoneum.

#### MICROSCOPICAL EXAMINATION

*Liver Parenchyma.*—There seems to be comparatively little healthy hepatic tissue left in the entire organ. In the rim of the cirrhotic liver lying between the large tumor and the capsule, the lobules are very hæmorrhagic. (Cf. Fig. 1, h, f.) In places where the process is not far advanced the central vein and capillaries are seen to be deeply congested and the liver cords well preserved only at the margin of the lobule. In many instances the process has seemingly gone much further, and the lobule appears as merely a mass of extravasated blood, all trace of liver cells being effaced. In some areas the cells show a compensatory hypertrophy. While the cords do not seem to deviate markedly from their normal arrangement, the cells are enlarged and irregular in form, and have frequently two or more nuclei which are likewise enlarged and take the hæmatoxylin stain very deeply. Such hypertrophied forms are described later in connection with the young nodules. (See Histogenesis.)

The nuclei of the capillary endothelium sometimes show a curious hypertrophy. They have become rounded or oval, stain very deeply with hæmatoxylin, and are sometimes so numerous as to fill the space between adjacent liver cords.

The olive green nodules which stud the left lobe prove to be necrotic liver tissue deeply bile-stained. Other necrotic areas are uncolored by bile.

The nodular appearance characterizing the whole of the left lobe (cf. Fig. 1) is due to an extensive new growth of fibrous tissue, which marks off areas of degenerated liver, as well as tumor nodules of various sizes, but does not tend to invade the individual lobules.

The fibrous bands reach their largest dimensions in the right lobe. (Cf. Fig. 1 b.) In this interlobular connective tissue one can determine an increase in "newly-formed bile ducts" which are occasionally widely dilated. The great length and narrowness which these duct-like canals sometimes show, together with the fact that they branch in a complicated way and even anastomose, seems strong evidence in favor of the view that they are really new-formed structures and not merely rows of compressed liver cells. In this instance, though they are very evidently continuous with well-defined bile ducts, their lining cells often become so flattened as to resemble thick endothelial cells. (Cf. Fig. 2.)

*Tumor.*—The neoplasm exhibits some diversity in structure.

The large mass (Fig. 1 a) proved entirely necrotic, so that its histological characters were obscured. Sections were made to pass through the areas marked d, h, j, g in Fig. 1, and in these the nature of the tumor could be studied. Very commonly when it is found as a nodule, and especially when it lies in a blood vessel, it consists of a mass of cords or strands lying side by side, and, as seen in longitudinal section, forming frequent anastomoses. (Cf. Fig. 3.) These cords vary in size, some consisting of but 5 or 6 cells in cross

section, others containing 50 cells or more. They are clothed by a delicate flat-celled endothelium. (Fig. 3 b.) A lumen, central or excentric, is occasionally seen—a mere gap between the surrounding cells, having no endothelial lining. (Cf. 4 c.) No bile was noted in these tubes, as was found by v. Heukelom.<sup>5</sup>

The spaces between the cord-like structures very frequently contain red blood corpuscles. (Cf. 3 c.) This phenomenon is easily understood in the case of the intravascular growths, where such spaces represent the lumen of the vessel. Where a tumor nodule is found in the midst of hepatic tissue, we may conceive that the blood spaces constituting the capillaries of the liver have persisted between the strands of tumor cells which spring from and correspond with the liver cords, as is described below under histogenesis. This conception explains also the origin of the endothelial covering of the strands. We have here the capillary endothelium which normally lies next to the liver strand.

Nodules of this description, varying from 2 or 3 mm. in diameter to a microscopic size, stud the left lobe, where they sometimes lie within a vessel wall, and again are immediately surrounded by liver cords. Transitions from liver cords to tumor columns were found in this region. (See Histogenesis.) The nodules here are in the main well-preserved. The small whitish dots (Fig. 1 g) consist of this cord-like form.

The well-preserved nodule (Fig. 1 d) gives a picture of larger and smaller masses almost invariably of this strand-like form, separated from one another by fine bands of connective tissue. There is occasionally a central necrosis, but in general the tissue is well-preserved here.

A second form exhibited by the tumor is somewhat more complicated. In this we seem at first sight to have a tissue made up of a very indefinitely arranged mass of cells. Closer examination reveals, however, elongated and irregular spaces (cf. Fig. 5 a) lined by a delicate endothelium (b) and containing blood corpuscles and fibrin (Weigert's fibrin stain). These spaces are further bounded by a row of cells, either polygonal and irregularly placed, or cylindrical and arranged side by side. Adjoining this row is a mass of irregularly arranged cells, beyond which one sees another row of polygonal or cylindrical cells, which, with a layer of endothelium, bounds another blood space.

Some of these spaces are not entirely walled off, but are continuous with the spaces described above as lying between the tumor cords. One may then conceive this part of the tumor to be made up of strands of cells branching and anastomosing very freely, and thus sometimes enclosing blood spaces with intact endothelium. The marginal cells of such cords generally retain a definite arrangement, while the central ones are rather disordered. Areas adjoining such a field as has been just described frequently show an absolute irregularity in the appearance and disposition of the cells. Giant forms with a single immense nucleus or with many large nuclei occur in such areas (cf. Fig. 7), and an

extensive fatty degeneration may be exhibited by all the elements, giving a spongy appearance to the entire field.

In the intravascular growth both forms of the tumor are seen, as well as the irregular areas with bizarre giant cells. Caseous tracts are also found here, showing sometimes faint outlines of tumor cords or lines of intact endothelium.

The vessel wall has its proper endothelium preserved, and that part of the tumor lying in apposition is similarly clothed. (Cf. also Fig. 6.)

Fragments of greenish bile are found in abundance both in the tumor cells and lying free in the spaces between them.

*Tumor Cells.*—In the strand-like form of the tumor (cf. Figs. 3, 4, 6) the cell body, as compared with that of a normal liver cell, is small, the nuclei in a tumor cord appearing more closely crowded than those in a liver strand. The shape of the cell is also modified, being moulded by the pressure of its neighbors to a polygonal outline. The protoplasm has the granular appearance of a liver cell, and in general is not bile-stained. The nucleus resembles that of a liver cell in size and appearance; is round or oval and contains many minute points of chromatin irregularly scattered and often joined together by fine strands. A larger mass of chromatin is frequently seen towards the centre. (Cf. Fig. 4.) Sometimes the cells in the outermost row in a cord, those lying next under the endothelium, have a denser cytoplasm and a more solid-looking, deeply-staining nucleus. (Cf. Fig. 6 d.)

With Mallory's stain the reddish-blue protoplasm has a vacuolated, granular appearance. The nucleus is provided with one or occasionally more oval or round bright red bodies containing vacuoles of relatively large size. At times the whole nucleus seems to be stained red, owing to the large size of this nucleolar body. In other instances, however, there is a space between the nucleolus and the nuclear membrane in which appear dots and strands taking the reddish-blue stain of the cytoplasm and the nuclear membrane. A hæmatoxylin stain does not differentiate between the various nucleolar bodies; all are stained blue.

In the second variety of the tumor (Fig. 5) much more irregularity in cell structure is seen. The cells bounding the blood spaces are frequently cylindrical in form and have oval or elongated nuclei (Cf. Fig. 6). The giant forms found here have already been referred to (Cf. Fig. 7). The nuclei in these cells are generally very dense, showing large irregular deeply-staining blocks against a ground filled with fine chromatin particles.

In portions of the tumor undergoing degeneration, the cytoplasm is often replaced by a fat globule, while the nucleus is very dense and assumes bizarre forms.

In certain of the young, fresh nodules seen especially in the left lobe, the nuclei show mitotic figures.

*Metastases.*—In the larger and smaller branches of the pulmonary arteries masses of the tumor are found as noted on naked eye examination. In the smaller vessels the growth is in general of the cord-like form and is fairly well preserved (Cf. Fig. 6). In the larger arteries the second

<sup>5</sup> Loc. cit.

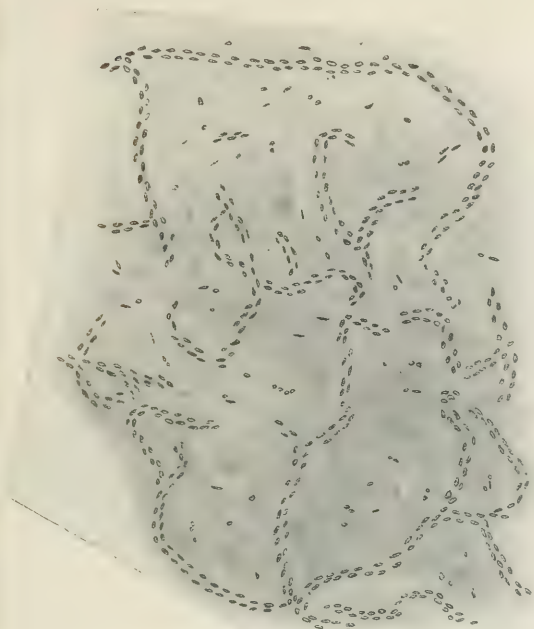
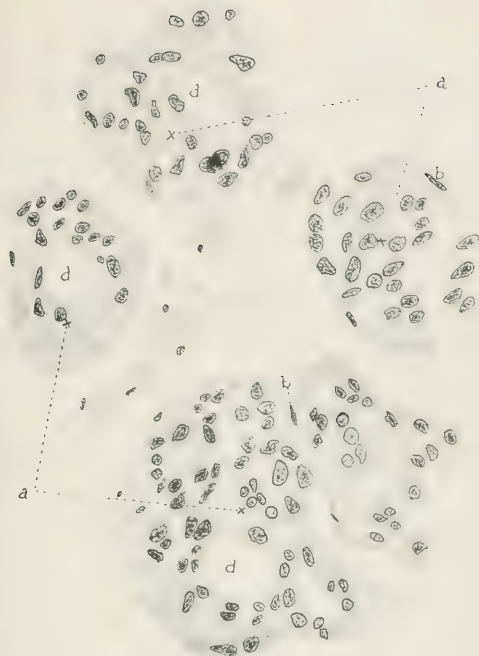
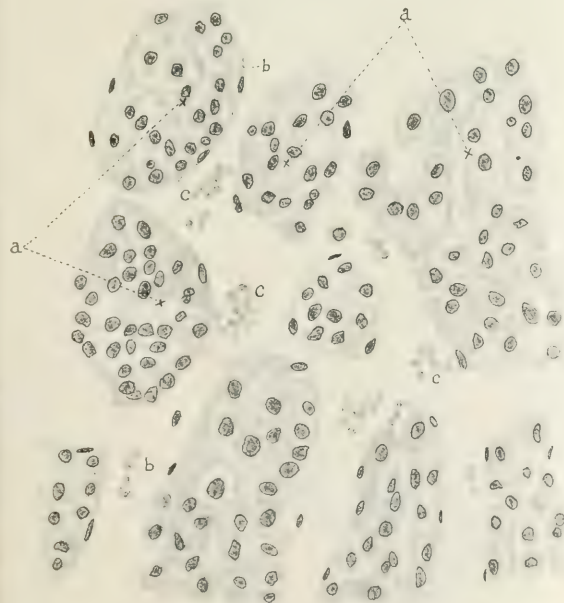
FIG. 2.—Connective tissue showing newly formed bile ducts.  $\times 112$ .

FIG. 4.

FIGS. 3 and 4.—Tumor. First form.  $\times 450$ .

*a.* Tumor cords. *b.* Endothelium. *c.* Red blood cells.  
*d.* Lumen.

FIG. 5.—Tumor. Second form.  $\times 85$ .

*a.* Blood spaces containing fibrin and red blood cells.  
*b.* Endothelium. *c.* Cylindrical cells.



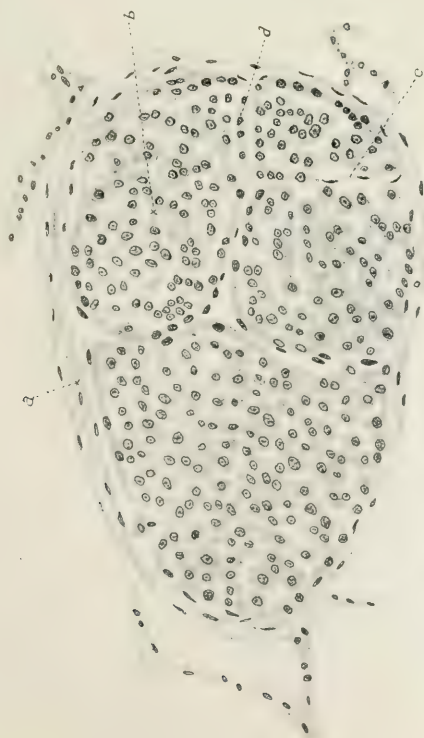


FIG. 6.—Tumor nodule filling pulmonary vessel.  $\times 112$ .  
*a*, Vessel wall. *b*, Tumor cord. *c*, Endothelium.  
*d*, Dense nucleus in marginal cell.

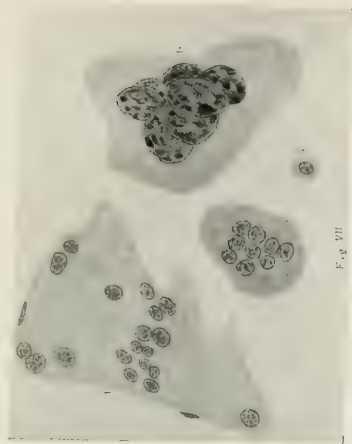


Fig. 7.

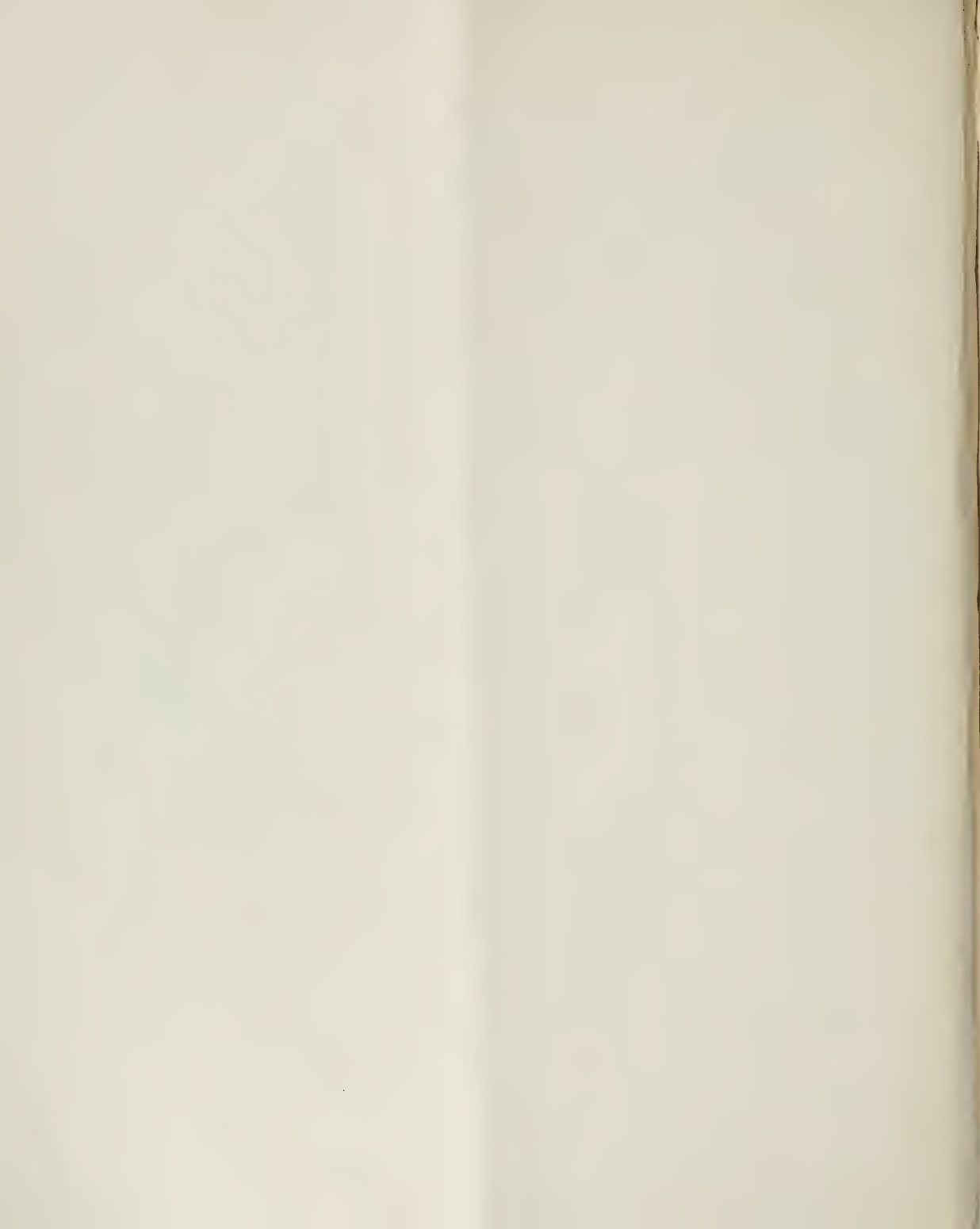
FIG. 7.—Cell forms from tumor.  $\times 300$ .  
*a*, Ordinary tumor cell.  
*b, c, d*, Multinucleated giant forms.



FIGS. 8 and 9.—Showing transition from liver to tumor.  $\times 600$ .  
*a*, Widened liver cords.  
*b*, Tumor cord.  
*c*, Endothelium.



FIG. 9.



form (Fig. 5) is also found; and here again disintegration and irregularity in the arrangement of the cells, and fatty degeneration are observed. The vasa vasorum in the walls of the larger vessels are frequently filled with the strand-like growth, and occasionally the tumor is found growing in the alveoli adjoining the vessels, sometimes forming large nodules.

Cloin<sup>6</sup> in his case found bile in the metastatic growths in the lung; none was observed in this instance.

*Histogenesis.*—This is best traced in young nodules (Fig. 1 h). The ground substance in which the nodules lie, the liver tissue, shows in the main such marked caseation that it is difficult to get an idea of its structure. The cells surrounding the nodules are generally in good condition, however. While it is not made out that the liver lobules become definitely enlarged, the cell-cords in the neighborhood of an area of new growth exhibit distinct hypertrophy, and in many instances the relation between liver cords and tumor strands can be traced. The nodule seems very often to have grown so exuberantly as to compress the cords of cells about it, giving them a squeezed appearance and concentric arrangement. The transition from these cords to the structures of the new growth is as follows:

The cells in the surrounding cords become larger, their nuclei are also enlarged and take a deep hæmatoxylin stain, and this widened atypical strand becomes still wider, comes to have several cells abreast, and passes thus gradually over into one of the cords definitely belonging to the tumor (Cf. Figs. 8 and 9).

v. Heukelom<sup>7</sup> gives exquisite pictures of just such a transition as that seen here, and Schmeiden<sup>8</sup> and Cloin<sup>9</sup> note a similar phenomenon.

Proliferation of the tumor cord thus produced can be readily conceived to give rise to nodules of larger and smaller dimensions as they are found all through the left lobe. Through anastomosis of adjacent cords the more complicated variety of the new growth may arise, as suggested above. The blood capillaries of the liver are evidently continuous with the spaces between the different tumor strands. The manifold small nodules scattered through the liver are then not of metastatic origin, but are primary growths derived by a direct transformation from the liver cells.

A word may be said here on the connection between cirrhosis and adenoma formation.

A few authors hold that the two processes are quite independent of each other. Many others think the coexistence of the two lesions is too frequent and too typical to be merely fortuitous. Some consider the adenomatous growth

the primary disturbance, the cirrhotic process being dependent thereon. On the other hand many hold that the cirrhosis is antecedent and the tumor growth a result. Owing to the destruction of liver parenchyma, due to an extensive new growth of connective-tissue, those liver cells which are intact undergo a vicarious hypertrophy. The large atypical cells thus produced are transformed in some way into adenoma cells.

A very rational view is suggested by the work of Marchand. That author found that after extensive destruction of the liver cells by some unknown poison (acute yellow atrophy) a connective tissue new growth accompanies the efforts at regeneration of the liver. These efforts are of two or perhaps three kinds, according to him: 1. The formation of large, irregular lobules from the lobules or portions thereof remaining. 2. The proliferation of cells—even degenerated ones—in the greatly degenerated areas. 3. The growth of bile ducts into the lobule.

In these cases of carcinoma of the liver the course may have been analogous. There has been a destruction of the liver tissue by some poison, to so great an extent that the organism is forced to undertake efforts at regeneration. These consist in the formation of atypical cell masses; and a further more atypical development of such masses results in the production of a malignant growth, the exact changes at this border-line between compensatory hyperplasia and malignancy being obscure to us. The cirrhosis is thus a phenomenon of invariable occurrence as part of the healing process after the degeneration of the liver, but is of quite secondary interest in the production of the tumor.

Orth<sup>10</sup> writes "One cannot help asking whether we have not here a vicarious hypertrophy which from some unknown cause proceeds past its goal and by atypical growth leads to the formation of a tumor," and Schmeiden<sup>11</sup> in a general way holds the same opinions.

As conclusions from the foregoing study we may state:

The case shows a multiple, primary neoplasm in the liver, accompanied by a widespread interlobular cirrhosis.

The new growth has invaded both portal and hepatic veins, and is found filling the pulmonary arteries and forming metastatic nodules in the lung tissue.

The tumor shows some variation in its structure, and transitions from liver cords to tumor strands are demonstrable.

The malignant tumor possibly results from the progressive atypical growth of hyperplastic masses produced coincidentally with the cirrhosis by a reparatory and regenerative process, after the extensive destruction of the liver by some unknown poisonous agent.

<sup>6</sup> Prager Medicinische Wochenschrift, XXVI. Jahrgang, S. 261, 275.

<sup>7</sup> Loc. cit.

<sup>8</sup> Loc. cit.

<sup>9</sup> Loc. cit.

<sup>10</sup> Loc. cit.

<sup>11</sup> Loc. cit.

## THE JOHNS HOPKINS HOSPITAL BULLETIN.

The Hospital Bulletin contains details of hospital and dispensary practice, abstracts of papers read, and other proceedings of the Medical Society of the Hospital, reports of lectures, and other matters of general interest in connection with the work of the Hospital. It is issued monthly.

Volume XII is now completed. The subscription price is \$1.00 per year. The set of twelve volumes will be sold for \$30.00.

## CONCERNING AN IMPROVED METHOD OF MAKING COLLODIUM SACS.

BY NORMAN MACLEOD HARRIS, M. B.,

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It will not be too presumptuous upon my part to state that by the majority of workers in our bacteriological laboratories both the utilization and the making of the collodium, or celloidin sac for experimental purposes is almost wholly neglected. This is largely to be accounted for, perhaps, either by the lack of a fully described technique of a reasonably easy method, or by the presentation of a too cumbersome method which entails spending too much time in overcoming many difficulties of a technical nature, thus naturally leading to discouragement and the abandonment of further attempts. It is, therefore, the object of this paper to present an improved method of making these sacs, the technique of which is simple and readily acquired, whilst the materials are practically always at hand in every laboratory for making them upon briefest notice.

Before entering upon details it may not, perhaps, be out of place to give a short review of the history connected with the introduction of collodium sacs and the several methods employed in their manufacture, so far as I have been able to get at the facts.

Taking advantage of the facilities for osmosis afforded by collodium films, the idea of sealing up bacteria in the living state within such films and placing them within the animal body to obtain, if possible, the effects of the elaborated diffusible toxins without the presence of the germs themselves in the blood or tissues, presented itself some six or seven years ago to Drs. Metschnikoff and Roux of the Pasteur Institute in Paris. This idea was successfully wrought out by them in their studies upon the toxins of Asiatic cholera in 1896, and later by Nocard and Roux who by this means undoubtedly isolated the causative factor of pleuropneumonia of cattle. This latter study was a veritable triumph, inasmuch as it *proved* what had heretofore been only suspected, that in certain infectious diseases we had to deal with living matter of such minute proportions as to be beyond the ability of the most powerful microscope to define.

Furthermore, Nocard was able by means of the sacs to transform the characteristics of the human tubercle bacillus into those of the avian variety, thus adding proof to the theory of the mutability of closely allied forms of bacteria.

It was also demonstrated that the virulence of pathogenic bacteria could in some instances be highly exalted by implanting a successive series of collodium sac cultures in the peritoneal cavities of animals.

Quite recently, McCrae has pointed out the value of the sac in the classification of bacteria of closely allied species, and produced agglutinative reactions in the blood of one animal inoculated with several sacs, each containing a different species of bacterium.

In perusing the writings of Roux, Metschnikoff and Nocard relative to their experimentations with collodium sacs, one curiously enough fails to glean the least hint as to how these sacs were prepared, nor do later publications from the Pasteur Institute seem to contain any references to the technique.

In this country some years ago (1898?) partially successful attempts were made by Dr. E. L. Trudeau of Saranac Lake to turn out a serviceable celloidin sac. He was, I believe, the first to suggest the employment of the ordinary gelatin capsule as a mold upon which to form the sac. The method used was found not to be sufficiently well developed to yield satisfactory results and publication was never made, although Dr. Trudeau openly spoke of his technique to many.

Dr. T. M. Prudden of Columbia University about the same time developed a method of making celloidin sacs by using a tube in whose bottom a small hole was blown, which previous to dipping was sealed by a thin film of celloidin. The tube was dipped in the medium and rolled until it had set, when the sac was dislodged by blowing into the tube, the air escaping from the small hole in the bottom and dissecting the film away from the sides of the tube. The method did not prove very satisfactory, nor did the coating of gelatin capsules in several ways yield any better results.

To Professor F. G. Novy of the University of Michigan belongs the credit of being the first to publish the method of Metschnikoff and Roux. This consists, briefly, in coating a glass rod of a certain thickness with collodium, several times, until a sufficiently thick layer is deposited, allowing it to set and then peeling the sac off by inversion, trimming it and affixing a piece of glass-tubing of proper calibre by the aid of gentle heat. By further manipulation the capsule is filled with broth, sterilized, inoculated and the tube sealed up close to the capsule by means of the gas flame.

Utilizing Trudeau's idea of employing the gelatin capsule as a mold, Dr. John McCrae of Montreal has devised a most successful method. His technique is briefly stated as follows: the larger end of a selected gelatin capsule is made to adhere to the end of a piece of glass-tubing of similar bore, by heating the latter a little. The capsule is then dipped in thin celloidin several times until a sufficient coating has formed, when it is further hardened by immersing in cold water. The gelatin is next dissolved away by hot water, the resulting celloidin sac filled with broth, sterilized, and preserved in a broth culture tube for use when desired.

Quite recently Dr. C. S. Gorsline of the University of Michigan has published a method which is essentially that of Prudden, but he has overcome difficulties of dislodging the sac from the glass tube by filling the latter with water

and forcing the water out through the hole by blowing into the tube. The sac is then fitted to a suitable piece of glass tubing by gently heating the latter, and the final technique is that of filling with broth and sterilizing under conditions suitable for preserving the capsule from contamination until required for implantation.

Regarding the method which I have devised, I can make few claims to any originality, having built upon Dr. Trudeau's idea of using the gelatin capsule, and benefited also by McCrae's efforts in the same line.

The procedure is carried out as follows, having first assembled the necessary materials consisting of—

(a) Empty gelatin capsules:—those of Parke, Davis & Co., may be had in the market, of almost any size desired, ranging from "No. 0—medical," holding about 1 cc., up to "No. 10—veterinary," holding approximately 30 cc.



FIG. 1.



FIG. 2.

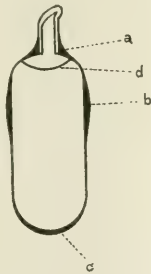


FIG. 3.

FIG. 1.—Empty gelatin capsule, actual size. "No. 12 Veterinary," P. D. & Co.

FIG. 2.—Glass tube sealed into end of capsule.

FIG. 3.—Sac ready for insertion. *a, b, c*, points of reinforcement; *d*, limit for height of the column of fluid inside.

(b) Glass-tubing:—preferably that having a gross diameter of from 2.5 mm. to 4 mm., or if such sizes are not at hand, coarser tubing may be drawn out to suit the purpose.

(c) Collodium (U. S. P.), or Celloidin:—either solution to be tolerably thick and kept in a small round jar, with closely fitting top, to the depth of 4 to 5 cm.

(d) A Drying-rack made by piercing a half inch pine board with rows of long fine wire nails at intervals of 4 cm.

(e) A glass-blower's burner, or some device to secure a long narrow flame.

(f) A small file.

*Procedure.*—Having selected the gelatin capsule, a piece of glass tubing 4 cm. long and of 3 mm. diameter is taken and the sharp edge of one end is filed down and that end heated a moment in the flame of a Bunsen burner, then the unseparated capsule is taken in the grasp of the left thumb and fore-finger, and with those of the right hand gentle pressure is made with the heated end of the tube directly against the centre of the end of the smaller portion of the capsule until the tube projects within the cavity not more

than 2 mm. (see Fig. 2). In a moment it becomes fast, if the heat has not been so great as to burn the gelatin, then one proceeds to apply a coating of collodium by means of a match or platinum loop around the junction point of tube and capsule. Now separate the capsule, and by means of a knife or other sharp-pointed tool clear the bore of the tube of the hardened cap of gelatin, then replace the two sections as before.

We now have the gelatin capsule centrally fixed to a permanent spindle which renders the coating with collodium or celloidin an easy matter. Before proceeding, however, to the coating process see that the collodium previously applied to the neck is quite dry. This being so, the jar containing the collodium is held tilted at an angle of about 50°, the gelatin capsule is slowly lowered into it and submerged sufficiently to coat the tube to the height of 1 cm. above the end of the capsule. It is now brought slowly up out of the collodium in the horizontal position quietly rotating it at the same time, care being taken not to remove too much collodium else the smoothness and evenness of the film will be interfered with.

Now rotate continuously until it becomes set, slowly at first to ensure an even distribution of the material, then more rapidly, blowing upon it occasionally to hasten the setting. I do not believe that immersing the capsule in water at this stage tends to any advantage, rather the reverse, for opacities are liable to develop in the film which may become permanent and spoil the transparency of the finished sac, and may be, prevent proper dialysation. When the film has set, the capsule may be placed at once upon one of the nails of the drying-rack to dry. It is of especial importance to let it dry out thoroughly. After this process is ended it is not necessary to repeat the coating unless the collodium is quite thin (I might say, here, that before using, I allow it to evaporate down to the consistency of a moderately thick syrup), for the thicker the film the less useful a sac becomes, however, after a trial or two each worker can use his own judgment as to what is enough. It is necessary at this stage to reinforce the sac at certain points, but before doing this it may be well to wind a piece of silk thread on the glass tube close to the capsule, tie it and leave two ends hanging so that the sac later on may be readily handled. Referring to Fig. 3, *a, b, c*, the points to be reinforced are indicated and the measure is carried out by means of the platinum loop, except in reinforcing the end which is accomplished by simply dipping the capsule again into the collodium. The sac is again placed upon the rack to dry, which occupies a short time, and it is then ready for the next step. In this way ten or twelve capsules may be set up in succession, and usually by the time the last one is coated the first will be found ready to be reinforced, and upon strengthening the last sac the first will be ready for finishing.

The gelatin must now be removed from the interior of the formed sac. This may go hand in hand with the sterilization, or constitute a separate procedure. Considering the

former proposal first, the coated capsule is removed from the rack and filled with broth by means of a Pasteur pipette, conveniently bent at right angles a little distance above the bulb, and at once placed in a broth culture tube, glass spindle downwards, and covered with broth to the extent of 1 to 2 cm. above the capsular end. The tube now holding the sac is autoclaved for five minutes at one atmosphere pressure and 120° C., thus rendering it completely sterile. It will be found upon removal from the autoclave that the gelatin has been melted and expelled from the sac and has gone into solution with the broth, so that we have now the sac filled with a medium of weak nutrient gelatin, which may congeal on cooling, constituting an excellent pabulum for bacteria.

If, however, it is thought to be desirable to remove the gelatin from the sac, the latter is to be filled as before, placed in a dish of hot water, when after a while the gelatin melts and may be washed out by means of the pipette, the process being repeated as often as is necessary. The sacs are then to be sterilized in the manner stated in the foregoing, and may be preserved in good condition for use at any time by leaving them in the culture tubes.

By the foregoing processes it will be found that very little, or no shrinking occurs in the sac if pains have been taken to dry it in the air after coating, and if the manipulations in coating have been deliberate no bubbles should be seen in the walls of the sac. Likewise, the glass spindle remains firmly fixed in position requiring considerable rough handling to cause its separation. It is surprising how tough such a sac can be after only one application of the thick collodion, and at the same time appear so frail.

As Novy points out, some varieties of collodion and celluloid are of little value for the manufacture of sacs on account of having such a low index of dialytic power, or are even without any, so it would be well to make a test of the osmotic properties of a sac before making a number of them.<sup>1</sup> This test can best be made by completely removing the gelatin and filling the sac with a saturated solution of magnesium sulphate, immersing it in distilled water and testing the latter for the presence of the salt at intervals.

The technique of inoculating and closing the sac will now be discussed. The culture tube containing the sterilized capsule is to be emptied of its fluid contents and the sac to be then deposited in a sterile Petri dish or some other suitable vessel. With a pair of sterile dissecting-forceps the glass spindle will be taken hold of and the sac held vertically upwards, whilst with a Pasteur pipette a small quantity of the contents is removed (see Fig. 3, *d*) so as to obviate any chance of the fluid within flowing up into the tube during the sealing of the glass, then with the pipette a small portion of the inoculating material is very carefully deposited within the

capsule, caution being needed not to permit any to touch the sides of the tube.

The sealing of the glass tube demands most delicate manipulation upon the part of the operator. Having prepared the glass-blower's burner, the spindle of the sac is taken hold of high up with another pair of sterilized forceps, and with the first pair (heated a little to disperse moisture from inside the tube near the site of sealing) a fresh grasp is to be taken lower down close to the junction of the sac and the tube, then with the sac held vertically the glass tube is brought into contact with the narrow non-luminous flame of the burner a short distance above the lowermost forceps, precautions being taken to first drive off any moisture which might be lodging at or near the point of sealing, the glass rapidly fuses and is drawn apart gently and the end attached to the sac sealed perfectly, as shown in Fig. 3. Care must still be exercised until the glass point is well cooled lest any agitation of the sac cause its contents to be thrown up into contact with the glass and crack it and render the sac useless. This danger being past, it is well to wash the sac off with sterile water or broth and replace it in a sterile broth culture tube until abdominal section has been performed upon the animal when it is removed and cautiously inserted and gently pushed away from the site of the incision by the sterile finger of the operator. McCrae very wisely suggests that at first the operator should incubate the inoculated sacs for 24 hours in broth to assure himself that there is no flaw in his technique of making the sac, and if the broth remains sterile then to proceed to insert the capsule in the animal; this procedure may be abandoned if it is seen that one has acquired the technique perfectly.

#### RESUME OF TECHNIQUE.

- (a) Preparation of the glass-tubing.
- (b) Fixation of same to gelatin capsule by heat.
- (c) Coating of junction-point while warm.
- (d) Clearing the bore of tube of gelatin.
- (e) Coating of the whole capsule.
- (f) Air-drying on the rack.
- (g) Reinforcing, and again drying.
- (h) Charging the capsule with broth.
- (i) Sterilization in autoclave (removal of gelatin).
- (j) Inoculation.
- (k) Sealing up glass tube.

#### ADVANTAGES OF THE METHOD.

1. There are practically no limitations to the size of the gelatin capsules requisite for experimentation.
2. There is no necessity to remove the sac from the mold, which is dissolved and forms a nutrient medium for the growth of the inoculated organisms.
3. A greater relative amount of dialysing surface is obtained by the use of a minimal quantity of glass, than is gotten by other methods.
4. By completely air-drying the collodion, a thinner, tougher, less shrunken and an equally good dialysing mem-

<sup>1</sup> I am, however, inclined to believe that the condition is more often caused by the water-hardening process, or by having too thick a film, than by the quality of the material.

brane is obtained than by the water-hardened, rod or tube systems.

5. The method seems to throw fewer discouraging difficulties in the way of the operator than most of the other schemes.

That the method is not perfect will occur to all, but I offer it in the hope that it will afford some the opportunity of accomplishing with less difficulty what has heretofore been one of the most involved of bacteriological technical procedures, and also the hope that it may finally lead some one to suggest a simpler and a more perfect method.

I take this opportunity to express my thanks to Doctors Trudeau, Prudden and Gorsline for information regarding their own technique.

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## PROCEEDINGS OF SOCIETIES.

### THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

*Meeting of November 18, 1901.*

Dr. Osler in the chair.

#### Arthritis Deformans. DR. BOGGS.

This man, 45 years of age, came in November 6, complaining of stiffness of the hips, back and neck. His family history is quite interesting in that his grandfather suffered with rheumatism and was disabled with stiff joints as was also his father and one paternal uncle. One sister also had rheumatism and tuberculosis, one of the etiological factors mentioned by Marie in this disease. His past history shows that measles was his only acute illness until he was grown up but he had lues at the age of 23; has never been addicted to the excessive use of alcohol.

His attacks began at 12 years of age with what he calls muscular rheumatism, that is, the joints were not affected but he had pains in the arms and legs near the joints without limitation of movements. By the time he was 15 he was unable to play in outdoor sports with the other boys because cold air brought on these attacks. These would sometimes be very severe for two or three days but he was not compelled to go to bed with them. When 24 years old he had his first severe joint attack, beginning in the right knee and extending down to the foot. Then it began in the left knee and foot, then changed back to the right and finally back to the left again. During this attack he lost 30 pounds in weight but in the course of three months was able to go about without the use of a stick. Shortly after this he noticed a stiffness and spasm in the abdominal muscles which gradually drew him over into a flexed position and his waist became so small that he could span it with his two hands.

This condition lasted for 15 years and about the time of the involvement of the abdominal muscles he began to have pain and spasm of the muscles of the eyes. These have persisted and at times are quite severe. During an epidemic of influenza in 1891 he had an attack, probably of acute articular rheumatism in which the feet and the hands became very much swollen. He has been getting worse since, the swelling being followed by pain and then after the acute stage by an increasing stiffness of the neck. At times there has been difficulty in swallowing. In 1894 he had another attack, this time affecting the hips, thighs and small of the back, the stiffness in the back increasing gradually until by 1896 the neck and back were rigid but there was slight motion still at the hips. There have been no acute attacks since but by 1898 he had lost entirely the power to flex the hips and assumed the characteristic position he now exhibits. Between 1896 and 1898 he noticed an increasing stiffness of the lower maxilla and at times he could not open the mouth sufficiently to take food, he used vigorous massage, however, prying his mouth open by one means or another and has regained some degree of motion of the jaws. He has no motion whatever in the spine now and the only motion left in the hip joint is a very slight degree of abduction when the legs are firmly pressed apart. The knee joints and ankles are perfectly free and he gets about with a fair degree of comfort but has difficulty in going up or down stairs. He is able to carry on his business as a lawyer.

The case is an illustration of one of the types of arthritis deformans described by Strümpell and Marie in which the spine is affected and sometimes the hips and shoulders. It is notable that the patient has none of the nodes of Heberden so common in another group of cases.

## DISCUSSION.

DR. OSLER.—This is one of an interesting group of some 5 or 6 cases we have had illustrating spondylitis deformans. This case in particular shows that the affection is only the spinal variety of arthritis deformans. This man has had recurring attacks of arthritis for many years. He has not the usual extreme nerve root pains but I judge the attack he had some years ago was due to pressure on the nerves as they passed through the foramina. Some of the cases have agonizing pains. One point that Dr. Boggs did not mention is the condition of complete ankylosis of the thorax which is a constant feature of this form.

Anatomically this is the oldest known disease. Skeletons with spondylitis deformans have been found among the mummies of Egypt.

DR. TINKER.—The surgical side of rheumatoid arthritis and arthritis deformans seems to be worthy of consideration because it offers the only possible means of relief for a very distressing deformity. Very little has been written about it, but from some recent reports it would appear that the condition is not quite as hopeless as it was formerly supposed to be. König has recently reported his experience in the treatment of 20 cases of this kind, with operation in four cases in which the hip was entirely ankylosed, as is the case here. He did resection with satisfactory results, all the patients being able to go about and at least two being able to take up their former occupations. Küster has also resected such joints with fairly satisfactory results. Some other writers have not been so fortunate and one states that he resected a joint which was quite painful with relief of the pain but without the patient being able to go about. In this country very little has been done in an operative way. Goldthwait, of Boston, has operated upon two cases with fairly satisfactory results by breaking up the ankylosis and following that with massage. In the earlier stages of the affection massage is probably beneficial and I believe this man has benefited himself very much by his exercises. After there is firm ankylosis the Germans believe that resection is the only thing to do.

#### The Question of the Operative Treatment of Acute Pancreatitis.

DR. BLOODGOOD.

(To appear later.)

#### A Case showing the Deformities of Chronic Gout. DR. FUTCHER.

The patient I have to show is one manifesting very advanced deformities in the joints as the result of chronic gout. The man is 54 years of age and was admitted the first time in 1894 complaining of pains in his feet, ankles and hands. There was no family history of gout. The patient had been a brick-layer most of his life but had been a brass-worker for a time after the onset of his gout symptoms. The first joint affected was probably one of the metatarso-phalangeal joints. This occurred about 14 years

ago. Every year from that time up to the date of admission he had repeated attacks of arthritis, involving at times also the elbows or the knees. He had been a heavy beer drinker, 2 or 3 pints a day and occasionally a glass of whiskey. The fact that he had been a brass-worker was probably of no special importance but whether or not lead was an etiological factor in his case it is difficult to say. For several years his joints have been markedly deformed and he has been incapacitated for work.

On admission to the hospital in 1894 he had an acute attack involving the hands and feet and there were quite marked deformities of the joints, but the nodules about the joints at that time were not definite enough to be called tophi. The first diagnosis was acute articular rheumatism with a question as to the possibility of gout. Since then he has been admitted 11 times, 10 times on the medical and one on the surgical side. The attacks of arthritis have been repeated and severe and the deposits about the joints have gradually increased in size. In 1897 he was admitted with a large swelling in front of the left patella. It was found that the prepatellar bursa was inflamed and required opening. On his second admission the nodules about the joints had become more definite and there were tophi in the ears. Microscopic examinations of these showed the characteristic acicular crystals of biurate of sodium and definitely established the existence of gout. As you see there are now enormous nodules over the knuckles of both hands. Occasionally these tophi suppurate and discharge their chalk-like contents. An interesting point in this case is that, as you see here on examination, there is a large collection of tophi over the sacral region.

As to the etiology, in this case, beer is probably the most important factor. There are four marked etiologic factors in gout: heredity in from 50 to 60 per cent, alcohol in a large percentage of cases; over-eating with insufficient exercise; and lead poisoning. Of our 32 cases of manifest gout, in a total of 14,000 cases seen in 12 years, practically all have given a history of alcoholism, fermented liquors—beer, ales and wines—playing a more prominent part than distilled liquors. It is rather interesting that ten of our 32 cases have given a history of having worked in connection with lead, a percentage which corresponds closely with Garrod's statistics. All of our cases have been in males and all in white patients. In 16 the diagnosis was established by the existence of tophi and in the others largely on the history and the fact that the attacks began with involvement of the toe joints. It is interesting that three of the cases, when first admitted, were diagnosed as acute articular rheumatism and it was only on subsequent admissions that the true diagnosis was established by the development of tophi in the ears or some other part of the body. Two of these had nodules beneath the skin which were at first considered to be the subcutaneous fibroid nodules of rheumatism, but which later proved to be tophi.

There have been three cases of gout with bursitis, two over

the patella and one over the olecranon; two suppurated and were operated on.

As to the definite disturbance of metabolism which is at the bottom of gout too little is known and it is impossible to go into the various theories at present, but it is in some way connected with the disturbance of uric acid metabolism and many adhere to the theory offered by Sir William Roberts some years ago. According to Bence-Jones and Roberts uric acid does not circulate in the blood as such but in the form of a quadriurate which is very soluble and easily eliminated. In gout, however, there is defective elimination or an excessive formation and the latter accumulates in the blood, in a medium rich in sodium carbonate. Eventually a molecule of the quadriurates is broken up into two molecules of acid biurate. The sodium biurate is very insoluble and is deposited in those tissues of the body where the circulation is poorest, the temperature lowest and the percentage of sodium chloride highest; in other words, in the cartilages and periarticular structures. This seems to be the most satisfactory explanation of the disturbance of metabolism in gout but the disease is still but poorly understood.

**A Case of Hæmorrhagic Pancreatitis. The Occurrence of a Fat-Splitting Ferment in the Urine.** DR. ORR.

The patient, a man 28 years of age, had before his fatal illness been in good health. There was no history of any previous digestive disturbance and he had never been jaundiced. His illness began four days before death with an attack of nausea and vomiting coming on shortly after a meal. About an hour later he was attacked with agonizing pain in the epigastric region, and the vomiting continued during the night but in the morning became less severe. The following day he suffered with violent hiccough, which continued until the time of operation. When admitted to the hospital he seemed very ill and vomited almost continuously. Examination of the abdomen showed nothing definite except distension in the neighborhood of the umbilicus. An exploratory laparotomy was performed by Dr. Mitchell and innumerable foci of fat necrosis were found studding the omentum. From this condition acute pancreatitis was believed to exist and an incision was made through the great omentum, between the stomach and transverse colon. The lesser peritoneal cavity was found to contain bloody fluid and the pancreas was covered by a coagulum of blood. It was not possible to obtain any evidences of a calculus in the gall bladder or in the bile passages and the abdomen was closed, a gauze drain being inserted in the upper angle of the wound. After the operation the patient vomited almost continuously—at first a dark brown fluid and later almost pure blood. He died on the fifth day of his illness, twenty-four hours after the operation.

An examination of the abdomen through the wound was permitted and it was possible to remove only the pancreas with the gall bladder and a portion of the duodenum. The pancreas is of great size, weighing 190 grms., the normal weight being only 90 grms. The head and tail of the or-

gan are firm and compact in texture and yellowish-gray in color, but the greater part of the body shows a hæmorrhagic lesion. Here the tissue is soft, of mottled red and reddish-black color, without the normal gland lobulation and has the typical appearance of hæmorrhagic pancreatitis. No gall stones were found in the gall bladder or gall ducts and the duct of Wirsung was not dilated. The parenchyma is the seat of widespread necrosis in the neighborhood of which the interstitial tissue is infiltrated with red blood corpuscles, polynuclear leucocytes and fibrin. The capillary vessels at the margin of the necrotic area shows the condition of hyaline thrombosis, observed in a case previously reported.<sup>1</sup>

Acute hæmorrhagic inflammation, as has been shown by Dr. Flexner and others, can be produced experimentally by injecting a variety of irritant substances, gastric juice, various acids and alkalies, suspension of bacteria, etc., into the pancreatic duct or into the parenchyma of the gland. I have shown that the same lesion can be reproduced in dogs by the injection of bile into the duct, and have described a case in which a gall stone in the diverticulum of Vater had caused the penetration of bile into the pancreas, this producing the lesion. In the present case it is not possible to demonstrate such an irritant. Unfortunately it was not possible to perform a thorough autopsy. A point of some interest is the occurrence of hæmorrhagic vomiting after operation, suggesting the presence of some lesion of the stomach, possibly a perforating ulcer in contact with the pancreas, thus permitting contact of gastric juice with the parenchyma. The suggestion unsupported by other evidence has little value but emphasizes the importance of a more complete post-mortem examination in explaining the etiology of hæmorrhagic inflammation of the pancreas.

In connection with this case it is of interest to consider the frequency with which gall stones accompany acute hæmorrhagic pancreatitis. In two of the cases examined in the Pathological Laboratory, gall stones were present. It is difficult to obtain trustworthy figures from the literature, since in many cases the autopsy reports are so meagre that the presence or absence of cholelithiasis cannot be determined. A considerable number of cases have been recently described by writers who have reported more than one case. Lund, of Boston, has reported five cases, three of which were examined after death, and in all of these gall stones were found. Bryant has reported two cases with gall stones. Hahn reports five cases, upon three of which an autopsy was performed; gall stones were found in one. Marx has described two cases with gall stones. Of these recently reported cases in which autopsies were obtained, in thirteen, including our three, gall stones were present in ten.

Since the diagnosis of acute lesions of the pancreas is difficult and at times impossible, the demonstration of a substance in the urine indicating such a condition would be important. Investigations of R. Langerhans and others have shown that disseminated fat necrosis accompanying

<sup>1</sup> Johns Hopkins Hospital Bulletin, 1901, Vol. XII, p. 184.

acute hæmorrhagic pancreatitis and other lesions of the pancreas is due to splitting of fat with the formation of fatty acid, and Flexner has demonstrated the presence of a fat splitting ferment in the areas of necrosis. It suggests itself that this ferment, which is free in the tissues may be excreted by the kidneys and for this reason I have made an examination of the urine in the present case. The results, though not conclusive, are worthy of attention, in order that similar examinations may be made in suitable cases. I used a method for the demonstration of fat splitting ferments, proposed by Prof. Castle and Mr. A. S. Loevenhart.<sup>2</sup> Ethyl butyrate, which is carefully purified, when acted upon by the ferment is decomposed with the formation of butyric acid whose presence is determined by litmus added to the solution.

Following the operation described the patient voided no

<sup>2</sup>American Chemical Journal, 1900, Vol. XXIV, No. 6.

urine and in the bladder at autopsy was found only a very small quantity. This was neutralized with potassium hydroxide and divided into two parts. To one part was added a few drops of ethyl butyrate together with a small quantity of litmus solution. The second part used as a control was boiled in order to destroy the ferment if present, and ethyl butyrate added. Both specimens were kept at 37° and at the end of twenty-four hours the unboiled specimen had acquired a well-marked acid reaction, while the control specimen was little if at all changed. Owing to the small quantity of urine obtained it was not possible to repeat the test which is described in order that its accuracy may be tested in other cases should the opportunity arise.

**Gonorrheal Peritonitis in a Child.** DRs. HUNNER and HARRIS.

(To appear later.)

## NOTES ON NEW BOOKS.

**Anatomy in its Relation to Art.** By GEORGE McCLELLAN, M.D., Professor of Anatomy at the Pennsylvania Academy of Fine Arts, etc., etc. (Philadelphia: W. B. Saunders & Co., 1901.)

This book of 112 pages with 125 plates which contain 333 illustrations, is intended to teach the artist the relation of the underlying structures to the surface of the human body, both in repose and in motion.

Anatomical knowledge is a very essential factor in the making of a true artist. In examining the annual output of the artistic profession of this country it becomes evident that the majority of painters and draughtsmen possess but vague ideas of the architecture of the human body.

The aid the camera affords has apparently been the factor causing the artist to partly abandon the excellent practice of the old masters, who studied by drawing free-hand from the model and the cadaver, thus determining in every portion of the body the causes producing the manifold characteristic forms. The camera undoubtedly has brought about a greater accuracy as to the contour and done away with many mannerisms of the old school, but it has also introduced a general indifference among artists when dealing with anatomical facts.

It is universally considered, that the most objective interpretation of nature is the best, because the artist's individuality is then least perceptible. This excuse is offered by those who wish to evade the trouble of studying anatomy; they say: "if one knows the causes for all the peculiar forms characteristic of the human body, one is very apt to overdo the detail work and represent nature not as she appears to our eye, but as our trained mind knows her to be." Then they quote great masters and great teachers and advise us to simply close one eye so as to do away with the confusing stereoscopic picture seen with two sound eyes and then proceed to copy nature "naïvely" and faithfully.

It is true that noble simplicity of form and outline has often been sacrificed for an exaggerated truthful anatomical representation of the human body; in other words, Beauty and Poetry are absent where the mathematical mind rules.

But this is not necessarily the case. The knowledge of anatomy in art is as essential for the proper representation of beauty in thought and conception as thorough bass is in

music and grammar in literature. To be sure, the anatomical knowledge of the artist should not be so much in evidence as to force itself upon the observer. All the landmarks of the bony framework of a figure should be in their proper places, though not all visible, and the muscles and tendons correctly attached, but there should be no exaggeration in detail, no muscle or fascia should be indicated unless it leaves an unmistakable protuberance or depression on the skin surface.

When studying from life, the artist is impressed with the great number of folds and depressions on the skin surface, some of which he presumes are constant, while others just happen to be there in his particular model. Clear anatomical knowledge will in such cases enable him to decide what is correct and typical, and therefore beautiful, and what should be regarded as an imperfection in the model. He knows at once how to discriminate between what ought to be imitated and studied and what discarded. Many of the best known artists of the past and of the present day must have had a vague conception of the healthy and normal human body, for they have often pictured figures as types of beauty or as their own ideals which showed slight, though unmistakable signs of disease, abnormal development or acquired deformities.

Every effort to teach anatomy to the artist is therefore a very commendable undertaking. There are many books on the subject, none of which are perfect. Those published by artists are generally worthless from an anatomical standpoint, while those written and illustrated by medical men give as a rule wretched pictures. It is true, that the artist can study anatomy better from the latter than from the former, but the teaching is by no means perfect. The bones, fascia and muscles composing a body, are not devoid of beauty in an artistic sense, and to portray them correctly a high degree of art is necessary, certainly more than one can expect of a pure scientist. The outlines of the individual bones for instance possess a characteristic grace, which the artist should be taught to see and appreciate, but if a book on anatomy pictures bones like pieces of rubber tubing joined together, the student must necessarily experience considerable difficulty in arriving at an understanding of the beauty of the human body.

The present contribution to our literature on Anatomy in

Art is a meritorious presentation of the subject; though it has the above-mentioned shortcomings. The author says in his preface that he "makes no pretension to enter the field of an artist, as it is only claimed that the drawings are diagrammatic expositions of the anatomy of the human body, where photographs would not serve the purpose," etc. These drawings are indeed very crude, and while they teach anatomy no better than it can be found in any of the standard text-books, their shapeless forms must have an undesirable effect upon the beginning art student. A book that is to analyze forms should at least picture them faithfully and with a suggestion of the three dimensions, even though only outlines be used, for a well-drawn contour is capable of indicating a form almost as correctly as an elaborately shaded picture.

The book contains not only drawings but also reproductions of photographs of two models, a male and a female, in different poses, which are quite instructive. They would be more so if the detail showed more plainly, a deficiency due probably to imperfect illumination of the model. As it is, the majority of these photographs appear more as grey silhouettes than plastic bodies. Moreover, the models employed show a number of deficiencies of form, which should have been especially mentioned in the legends, so as to avoid the risk of impressing imperfect forms upon the memory of the student.

The best pictures and the most instructive are three views of Houdon's famous statue "L'Écorché"; the accompanying three poses of the male model used in the book, which are in the same position as the statue, seem superfluous. The same can be said concerning other similar poses, although as said above, a number are quite useful and a full-fledged artist, having the gift of discrimination will undoubtedly enjoy studying them.

The text is clear and concise and it gives much that is interesting to both artist and anatomist. The different chapters are short. After an introductory note we find descriptions of: the skeleton—articulations—bones of head and face, muscles of head and face—the neck—the trunk, thorax, abdomen, back—the upper extremity—the pelvis—the lower extremity—general considerations of the entire skeleton—influence of the skeleton on the surface form—influence of the muscles on the surface form—attitudes and postures—movements of progression—proportions of the human figure.

The book is rendered voluminous by the great number of plates, while the text is so concise, that it may be read in one sitting. The book is well made and aside from the fact that the text is printed in gray, the pages look well.

**Gynecological Pathology. A Manual of Microscopical Technique and Diagnosis in Gynecological Practice for Students and Physicians.** By DR. CARL ABEL, Privat-Dozent in Berlin. Translated and edited by Samuel Wylis Bandler, M.D., Adjunct Gynecologist of the Beth Israel Hospital, New York, with a chapter on the Embryology of the Female Genitalia and the Pathological Growths developing from Embryonal Structures. Illustrated by 100 engravings. (New York: William Wood & Co., 1901.)

The first chapter is devoted to the method of obtaining uterine tissue for diagnosis. In the first place we would mention that if the speculum advocated be used perfect asepsis is almost out of the question, as we are advised to fasten the speculum to the table. Then again when pieces of cervix are examined the bleeding is usually checked by packing with cotton; where any appreciable amount of tissue is removed it is always better to approximate accurately with sutures instead of leaving the tissue to granulate. We are pleased to note the careful macroscopical examination of scrapings and

we are advised to make frequent use of the magnifying glass. Many cases of malignant growth may undoubtedly be recognized in this manner. The various methods of cutting and staining are briefly and yet clearly given. Abel finds it necessary to leave a uterus in Müller's fluid from six to eight weeks before sufficient hardening has taken place. If he placed the specimen in the thermostat and changed the fluid whenever it became cloudy less than two weeks would be the requisite period. His remarks on so-called erosions of the cervix and also on the eversions of the cervical mucosa are very clear and to the point. The confusing and suspicious pictures occasioned by the irregular and yet benign dippings down of the normal cervical epithelium are carefully dealt with. Squamous-cell carcinoma and adeno-carcinoma of the cervix are, however, not very clearly depicted and from them the student will gain but a hazy idea of the various stages of the disease. Hyperplasia or as we are accustomed to term it hypertrophy of the mucosa is well described and suitably illustrated. But cancer of the body is allowed but little space, although it is exceedingly important. In summing up the description of carcinoma of the body of the uterus Abel says "the deep extension of the glandular neoplasm into the muscle is then the only criterion of the malignancy of the neoplasm." Were the author right in his assumption we would be in a sorry plight. In the early stages of the disease the curettings rarely yield muscle and it is only in the fairly advanced and late stages that muscle is found in the tissue removed by the curette. Abel directs little or no attention to the atypical gland grouping and to the pathological changes in the individual cells. These are the true factors in the diagnosis and from them alone the diagnosis can be made in nearly every case. Of course if muscle be present we have additional confirmatory evidence but this is not at all necessary. Uterine myomata and also dermoid cysts are treated in a very cursory manner, the former not being accorded even one page. Inflammations of the tube are fully and very satisfactorily described and the description of tubal pregnancy is undoubtedly the best in the book. The anatomy of the ovary is very clear but the descriptions of pathological conditions meagre. Abel mentions having found small cyst-like spaces lined by giant cells in a dermoid cyst of the ovary. Little attention has been paid to this in the past. We have found them repeatedly in dermoid cysts. In fact, they are undoubtedly pathognomonic of dermoids and whenever we have found them in the ovary further sections revealed the presence of a dermoid no matter how small the cyst was.

Undoubtedly the most interesting portion of the book is Part III, which has been added by the translator. Bandler has given us a very clear idea of the embryology of the female genitalia and has been most judicious in his selection of illustrations from the various monographs on the subject. He has also given us a full survey of the pathological growths developing from the embryological structures, paying especial attention to adeno-myomata.

The text on the whole is clear, but in several places some obscurity exists, for example, on page 67: "At times there develops in a carcinoma an adenoma above the remaining epithelium of the cervical mucous membrane, i. e., the glands so that a mixed tumor results (adeno-sarcoma)." We presume that the word carcinoma instead of sarcoma has been accidentally inserted, but even then it will be rather difficult for a skilled pathologist to get his bearings.

The illustrations in part are very good, but many, while presenting a general idea of the histological picture, on careful scrutiny fail to give the finer details so necessary for the student.

The Four Epochs of Woman's Life. A study in Hygiene. By ANNA M. GALBRAITH, M.D., Fellow of the New York Academy of Medicine, etc. With an Introductory Note by JOHN H. MUSSEN, M.D., University of Pennsylvania. 12mo. volume of 200 pages. (Philadelphia and London: W. B. Saunders & Co., 1901. Cloth, \$1.25, net.)

This book is written by a woman physician for women who are supposed to be unacquainted with the essential facts of their sexual life. It seems upon the whole judiciously written, although there is at times too much technical knowledge for the unscientific reader and too little for the thorough student. A tendency is noticeable which is not altogether absent from similar semi-scientific and semi-popular works written by women to enter upon discussions which have but a remote, if any, connection with the subject-matter of the book. Thus the present book commences with a brief essay upon education and the correlation of mind and body. The views presented are unimpeachable and in fact are derived from standard authors, but they seem out of place in a treatise whose avowed object it to teach woman about her sexual system. The book otherwise is clearly and properly written and seems well calculated to instruct young women, especially young wives and mothers in matters which they ought to know.

First Aid to the Injured and Sick. By F. J. WARWICK, B.A., M. B. Cantab., Associate of King's College, London; Surgeon-Captain, etc.; and A. C. Tunstall, M.D., F.R.C.S. Ed., Surgeon-Captain, etc. 16mo volume of 232 pages and nearly 200 illustrations. (Philadelphia and London: W. B. Saunders & Co., 1901. Cloth, \$1.00 net.)

This compact, handy and useful manual can be recommended to all who are called upon to meet sudden accidents or emergencies. The chapters on bandaging, the immediate treatment of hemorrhage, artificial respiration and the transportation of the wounded are especially valuable. The directions given are clear and easily understood.

Outlines of Anatomy. A guide to the methodical study of the human body in the dissecting room. By EDWARD W. HOLMES, A.B., M.D., Demonstrator of Anatomy, University of Pennsylvania, etc. Second edition. (1902. Press of the New Era Printing Co., Lancaster, Pa.)

The intention of this manual of less than two hundred pages is to introduce method and discipline into the dissecting room and to awaken an interest in practical anatomy. The course of dissection laid down is designed to consume twenty-eight days, which would seem to be a minimum requirement for practical anatomy. The book is good but elementary and the impression which it leaves upon the reader is that the author in his teaching sought to teach anatomy rather than to make anatomists. The purpose of the book is excellent even if the standard is not high.

Essentials of Physiology. Prepared especially for Students of Medicine; and arranged with questions following each chapter. By SIDNEY P. BUDGETT, M.D., Professor of Physiology, Washington University, St. Louis. 16mo volume of 233 pages, illustrated. (Philadelphia and London: W. B. Saunders & Co., 1901. Cloth, \$1.00 net.)

An excellent and probably the distinguishing feature of this compend is the chapter on the nervous system which is fully

illustrated by half-tone reproductions of schematic representations of various parts of the brain and spinal cord. The book as a whole is marked by clearness and conciseness of statement and if one needs a question compend this may be recommended as a reliable and modern guide.

## BOOKS RECEIVED.

A *Text-Book of Surgery*. By Dr. Hermann Tillmanns. Translated from the seventh German edition by Benjamin T. Tilton, M.D., and John Rogers, M.D. Edited by Lewis A. Stimson, M.D. Volume I. The Principles of Surgery and Surgical Pathology. With five hundred and sixteen illustrations. 1901. 8vo. 841 pages. D. Appleton and Company, New York.

A *Treatise on the Acute, Infectious Exanthemata*. Including Variola, Rubella, Scarlatina, Rubella, Varicella, and Vaccinia, with especial reference to Diagnosis and Treatment. By William Thomas Corlett, M.D., L.R.C.P. Lond. Illustrated by 12 colored plates. 28 half-tone plates from life and 2 engravings. 1901. 8vo. 392 pages. F. A. Davis Company, Philadelphia.

A *Text-Book of Physiological Chemistry*. For Students of Medicine and Physicians. By Charles E. Simon, M.D., 1901. 8vo. 453 pages. Lea Brothers and Company, Philadelphia and New York.

*Twenty-eighth Annual Report of the Secretary of the State Board of Health of the State of Michigan*. For the fiscal year ending June 30, 1900. 8vo. XXVII + 272 pages. 1901. Lansing, Michigan.

*Transactions of the State Medical Association of Texas*. Thirty-third annual session held at Galveston, Texas, April 23rd to 26th, 1901. 8vo. 463 pages. Austin, Texas.

*Transactions of the Clinical Society of London*. Volume the thirty-fourth. 1901. 8vo. lx+270 pages. Longmans, Green, and Company, London.

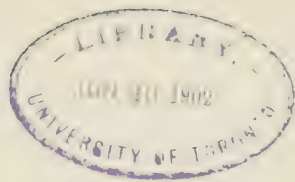
*Transactions of the American Surgical Association*. Volume the nineteenth. Edited by Richard H. Harte, M.D. 1901. 8vo. xxviii+514 pages. Printed for the Association. Philadelphia.

*Water and Water Supplies*. By John C. Thresh, D.S.C. (London); M.D. (Victoria); D.P.H. (Cambridge). Third edition, revised and enlarged. 1901. 12mo. 527 pages. P. Blakiston's Son and Company, Philadelphia.

*Laboratory Work in Histology*. By G. Carl Huber, M.D. Third edition, revised and enlarged. [1901.] 8vo. 204 pages. George Wahr, Ann Arbor, Michigan.

*Epilepsy and Other Chronic Convulsive Diseases*. Their Causes, Symptoms and Treatment. By Sir William R. Gowers, M.D., F.R.C.P., F.R.S. Second edition. 1901. 8vo., xxiv + 320 pages. P. Blakiston's Son and Company, Philadelphia.

*Medical and Surgical Reports of the Boston City Hospital*. Twelfth Series. Edited by Herbert L. Burrell, M.D., W. T. Councilman, M.D., and Charles F. Withington, M.D. 1901. 8vo. 201 pages. Published by the Trustees, Boston.



# BULLETIN

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## ACUTE GENERAL GONORRHEAL PERITONITIS.<sup>1</sup>

BY GUY L. HUNNER, M. D., *Resident Gynecologist, The Johns Hopkins Hospital,*

AND

NORMAN MACL. HARRIS, M. B. (TOR.), *Associate in Bacteriology, Johns Hopkins University.*

It is probably universally admitted to-day that the gonococcus is capable of being the sole cause of an acute general peritonitis. In May, 1899,<sup>2</sup> Dr. H. W. Cushing read a paper before the Johns Hopkins Medical Society reporting what he then supposed to be the first cases to conclusively prove

this proposition. We have since found that two authors, Frank, of Louisville, in 1895, and Mejia, of Paris, in 1897, antedated Cushing's report with cases which rest upon convincing bacteriological work.

As Cushing pointed out, it is to Wertheim we owe the credit for first demonstrating that gonococci can live upon the human peritoneum. In 1892 he operated upon a case of salpingitis with extensive acute pelvic peritonitis; and, from the peritoneal exudate, he demonstrated the gonococcus both on cover-glass and in culture. He had already created acute localized inflammatory processes in the peritoneum of ani-

<sup>1</sup> Presented before the Johns Hopkins Hospital Medical Society, November 18, 1901.

<sup>2</sup> The bacteriology of these two cases may be found reported *in extenso* by Dr. H. H. Young in his contribution to Welch's "Festschrift" entitled, "The Gonococcus," The Johns Hopkins Hospital Reports, vol. ix, p. 686.

imals, and successfully recovered the living organism in pure culture from such areas of peritonitis.

While the etiologic rôle of the gonococcus may now be considered as conclusively proven, the questions of prognosis and treatment are still unsettled.

The following case is reported to emphasize the relative frequency and gravity of this condition in children.

The patient, M. V., a child 10 years of age, was admitted to Dr. Kelly's service from the dispensary on Nov. 4, 1901, with the message that she had a gonorrheal vaginal discharge and probably a peritonitis. The following history was obtained from the mother: On Saturday, Oct. 26, the child complained of soreness about the external genitalia and was instructed to wash the region and to put on fresh underclothing. On Monday, two days later, she was taken with abdominal pain, cramp-like in character, for which her mother massaged the abdomen and gave a dose of salts. On Tuesday morning the child returned from school because of abdominal pain, vomiting, and a constant desire to defecate with no result. In doing the week's washing on Wednesday the mother discovered a staining and stiffening of the child's undergarments, and for this reason brought her to the dispensary on Thursday, Oct. 31. The dispensary note says the child was pale, ill-looking, and complained of pain over the symphysis, and of painful micturition. There was a purulent vaginal discharge which microscopically showed many pus cells and many diplococci with the morphology and arrangement typical of gonococci. A potassium permanganate douche was ordered and the child was not seen again until Monday, Nov. 4, the day of admission. Her mother stated that in the meantime the abdomen was swollen and hard, and that the child walked about in a bent-over position. She knew of no gonorrhea in other members of the family, and had not questioned the child about coitus.

The patient was admitted at 5 p. m. with a temperature of 99.8° F. and pulse 104. When seen at 7 p. m. she was lying in dorsal decubitus, with legs naturally extended. Her cheeks were slightly flushed but she did not appear feverish. There was no anxious expression, and she seemed mentally bright and cheerful. She said she had had a bad "stomach ache" and some vomiting in the morning, but she felt well now. Her tongue was slightly covered with a diffuse grayish coating. Her pulse was 100, regular, and of good volume. Her abdomen was somewhat distended, cylindrical in outline, the costal grooves being obliterated. Her respirations were costal but she readily took deep abdominal inspirations without pain. On being asked to indicate the site of her morning "stomach ache" she placed her hand over the hypogastrium. On palpation the entire abdomen was resistant, but fairly deep pressure could be made without complaint of much pain. On percussion the note was generally dulled, but resonance was everywhere present except in the right flank, where there was dullness which changed to Skodaic resonance on turning the patient to the left side. In the left flank the note was high-pitched and remained the same on turning the patient to the right side.

We were dealing then with a child who had gonorrhea for an unknown period and a very suggestive history of peritonitis for one week. The physical signs of a positive nature were moderate distention, muscle rigidity, and some complaint of pain on deep pressure in the hypogastrium. Her excellent pulse, good mental condition, and general appearances led us to believe that we were dealing with a general peritonitis of gonorrheal origin which had spent its force and was now in the process of healing. An operation was not thought to be

indicated. During the night, however, a decided change took place, and when seen at 9 o'clock the following morning the patient presented an entirely different picture. Her expression was anxious and her face was drawn and very cyanotic. The patient was very restless and complained of thirst. Her temperature was 100.2° F. and pulse 144. The pulse was soft, bounding, and easily compressed. The tongue was thickly furred and the breath foul. The abdominal condition was about the same. At 11 a. m. the temperature was 103.2° and the pulse 136. The leucocytes were 10,000 at 1 p. m.

The consent of her parents to an operation could not be obtained until 2 p. m. In the meantime hot turpentine stupes were applied every half hour to relieve the abdominal pain which had become very severe early in the morning.

*Operation; Dr. Hunner, Nov. 5, the ninth day of peritonitis: bowel toilet, irrigation and closure.* During an examination under ether, the muscle rigidity persisted; no absolute demonstration of movable dullness. The vaginal mucosa was congested. The hymen had been dilated, and readily admitted the little finger. Rectal examination showed a uterus of about normal size, but the adnexa could not be distinguished. No definite mass in the pelvis. The abdominal incision was made rather high to avoid the bladder. The peritoneum was congested and edematous. Its incision revealed a slight increase in the peritoneal fluid, which was chocolate red in color, and turbid with a grayish flaky-looking material.

The omentum was congested and adherent to the anterior abdominal wall and to the intestines. The intestines were slightly distended, congested, adherent to each other and to the lateral peritoneal surfaces.

Three centimeters of the appendix could be seen projecting from a retrocecal pouch. It was seven millimeters in diameter and normal except for the congested serosa. A large loop of ileum fell from the ileocecal valve region down into the right pelvis. The right tube was adherent to the pelvic wall and swung around posterior to this loop of ileum, its fimbriated end being attached to the rectum. On freeing the end a patch of white fibrin was left on the rectum. No pus could be squeezed from the tube. The left tube was adherent to the infundibulopelvic ligament, its fimbriated end being open, and yielding no pus on pressure. The ovaries were fetal in type, swollen, and semi-translucent. Beginning at the ileocecal valve the small bowel was taken up loop by loop and its coating of fibrinous material wiped off with wet gauze. On reaching the splenic region considerable purulent material was encountered, and an attempt was then made to cleanse the cavity with a saline irrigation, six litres being used while the upper intestines were being gently wiped.

The mesenteric glands were everywhere swollen and in the upper abdomen they were deeply hemorrhagic.

The abdomen was left full of salt solution and closed with interrupted silkworm gut sutures. The skin was thoroughly Paquelinized, and four ounces of epsom salts were left in the rectum.

The patient died thirty-six hours after operation, her condition in the meantime being, as before operation, one of extreme prostration. She complained of great thirst and of pain in the upper abdomen. She drank large quantities of water and vomited frequently. The bowels moved freely and the abdominal condition seemed about as before operation. Her temperature ranged between 99° and 100° F., and the pulse, of very poor quality, was counted between 130 and 160. Frequent saline infusions and coffee enemata, with high strychnia stimulation, failed to change the picture from that of a profound toxemia.

At the operation cultures and coverslips were taken from

various regions in the abdomen. Dr. Harris will speak of these and of the autopsy findings.

**Pathological Report.** Autopsy No. 1819. M. V—, æt. 10 yrs., white. From the service of Dr. Kelly, ward H.

**Anatomical diagnosis:**—General adhesive peritonitis. Salpingitis. Fatty degeneration of liver. Anemia. Bronchopneumonia.

The autopsy was performed by Dr. Yates 6 hours after death on the 7th of November.

The body is that of a fairly well-nourished girl 138 cm. long, and is considerably jaundiced. There is slight rigor mortis present, also anemia. There is a slight vaginal discharge, the hymen is dilated, and in one or two places jagged. No pus can be squeezed from the urethra. Bartholin's glands are not enlarged. In the mid line of abdomen is an incision 15 cm. long extending upwards from the symphysis pubis.

**Peritoneal Cavity:**—Upon opening the peritoneal cavity there are found to be general adhesions. The omentum is adherent to the line of incision, especially where the stitches still hold, and on the posterior surface it is strongly bound to the subjacent intestines; there are no adhesions in the anterior omentum. On separating these off from the intestines, isolated abscesses were found, none of which were found in the upper portion. At the left lateral margin of the omentum, straw-colored serous fluid is found in considerable quantity. The intestinal adhesions are all below the omentum and are especially marked in the pelvis. Above the omentum the stomach, spleen, liver and the under side of the diaphragm are found to be covered with a dry plastic exudate, there are, however, no definite adhesions. The lesser peritoneal cavity is slightly, or probably not at all involved. The adhesions between the coils of intestines are fairly firm, as are also those between the omentum and the intestines.

**Thorax:**—The pleural cavities contain no excess of fluid. The lungs are free from adhesions. At the upper posterior margin of the lower lobe of the right lung, and at the posterior margin of the left lung are irregular, raised, dark areas over which the pleuræ are smooth. The surfaces are very nodular in appearance. On section, corresponding to these triangular-shaped areas of hemorrhages are found mottled diffuse nodules 3 cm. in diameter. Portions of these when excised show no tendency to sink in water. No pus is evident in these areas. In the bronchi is some blood-stained mucus, otherwise the condition is normal. In other respects both lungs present similar conditions of slight hypostatic congestion, but crepitation is everywhere present.

**Heart** appears normal.

**Liver:**—Weighs 850 grs., measures 21 x 15 x 7 cm. The serous surface, especially that of convex surface of the organ is covered for the most part with dry granular lymph. The organ is not enlarged and the entire surface shows a peculiar red and yellow mottling corresponding to the lobulation. On section, the cut surface presents at first glance a typical "nutmeg" appearance, but closer inspection makes it seem that the centers of the lobules are yellow and the peripheries red.

**Gall-bladder** and ducts seem normal.

**Spleen:**—Weighs 100 grams, measures 10 x 6.5 x 3 cm. It is slightly enlarged and firm, and the capsule is wrinkled. The cut section shows a reddish-brown color. The Malpighian bodies are very prominent and translucent. The trabeculae are not increased.

**Kidneys:**—Combined weight 250 grams. They are of about the same size and appearance. The left one shows well-marked fetal lobulation. The capsule strips off leaving a smooth surface. The stellate veins are considerably injected. Cortical striations are much obscured by apparent swelling of the

epithelium. Thickness of cortex 8 mm. Dimensions of organ, 10 x 5 x 3.5 cm.

**Urinary Bladder** seems normal.

**Genitalia:**—The Fallopian tubes are apparently enlarged and a mucoserous fluid can be squeezed from the free end of the left tube, as also on cross-section.

The uterus is not enlarged, its cavity is free and contains no pus.

The ovaries, beyond adhesions, show no apparent change.

The vagina is slightly injected, smooth and shining and has no apparent granular inflammation.

**The Stomach:**—This organ is considerably injected, its serous surface is dry and no longer glistening.

**The Intestines:**—They are slightly injected, but not constantly so, and aside from the adhesions they seem normal.

**The Aorta** seems normal.

At the time of operation, cultures and coverslip preparations were made by Dr. J. Butler, who reports as follows:

The cultures were made upon slanted pleuritic-fluid-agar from several locations in the abdominal cavity, namely, Douglas' cul-de-sac, region of the splenic flexure of the colon, and from amongst the coils of small intestine. All cultures but that from the latter situation proved sterile, this tube-culture presented three round, elevated, opaque-white, smooth, moist, glossy colonies, whose diameters were about 2 mm. These colonies yielded a staphylococcus which stained by Gram's method and had not the morphological characters of the gonococcus. Upon further investigation it was proven to be *Staphylococcus cereus albus*.

From the above-mentioned areas coverslips were likewise made and subjected to careful scrutiny, with the result that none showed any bacteria, excepting that taken from amongst the coils of the small intestine, which exhibited only a scattered group of micrococci staining by Gram's method and corresponding in their morphology to those isolated by culture from the same location. Nothing suggestive of gonococci was seen."

Upon the body coming to autopsy, plate cultures were made in hydrocele-fluid-agar from the heart's blood, bronchopneumonic areas in the right lung, spleen, uterine cavity, right Fallopian tube, the urinary bladder, and from two areas in the abdominal cavity, namely, the right flank below the liver, and centrally, amongst the coils of small intestine. The plates were incubated in the thermostat for 48 hours at 36.5° C., and then carefully examined, yielding in the last analysis the following organisms:

1. *Micrococcus gonorrhæ* from both localities chosen in the peritoneal cavity.

2. *Streptococcus pyogenes* from the heart's blood, uterine cavity, urinary bladder, and bronchopneumonic areas in right lung.

3. *Bacillus coli communis* from the heart's blood, uterine cavity, right Fallopian tube, urinary bladder, and peritoneal cavity (both sites).

As especial interest is attached to the isolation of the gonococcus, a few words may be said in regard to the facts shown by culture and coverslip preparations which led up to its positive recognition. The plate made from the purulent exudate in the right flank presented two types of colonies with the following characteristics: type (a), present both on the surface and in the depths of the medium and very numerous. To the naked eye the surface colonies had an average diameter of 1.25 mm., they were round, slightly elevated, gray, translucent, moist, smooth and glossy; whilst under the low power of the microscope they seemed to be perfectly regular in outline, translucent, straw-yellow color, very finely granular, and frequently possessing a nucleus of a round or oval character. To the unaided eye the deep colonies were very small and pre-

sented nothing typical, but under the microscope they were found to be irregularly round or oval, granular, and of a brown-yellow color. Type (b); these colonies were six in number, and were large, white and ovoid, having the usual appearance of colonies of the type of *B. coli*, as such they proved to be. The plate from the central intestinal area yielded only one colony of type (a), but a large number of type (b).

These small colonies when removed for preparing coverslip specimens were found to possess a very definite degree of viscosity, clinging strongly to the needle and not mixing readily with the water on the coverslip during the spreading process. When stained, such preparations were made up of cocci which were larger upon the average than the usual pyogenic cocci, varying considerably in size and in intensity of reaction to the aniline dyes. They were usually grouped in more or less reniform shape as pairs, or in some cases the line of division between two cocci was quite straight, tetrads and clusters were also frequent. Gram's method of staining yielded entirely negative results. Attempted growth on any of the ordinary laboratory media always ended in failure.

All other plate cultures gave no evidence of the presence of this micrococcus, although diligently sought for.

Likewise the coverslip preparations made from the peritoneal exudate in the right and left flanks, respectively, the uterine cavity, and the right Fallopian tube were stained and carefully gone over, to detect if possible the presence of gonococci. The only positive result was obtained from the coverslip smear made from the exudate in the right flank. This showed abundance of polymorphonuclear leucocytes, a few mononuclear cells, both large and small, some fibrin and multitudes of micrococci which occurred singly, in pairs, in tetrads and in clusters, varying in size and more often extracellular, although one could readily find leucocytes holding from two to twenty cocci. The reniform shape of the diplococci was not always observed, especially when extracellular. Gram's method of staining did not yield entirely uniform results, due without doubt to some fault in technique, as some streaks running across the field would give complete decolorization, whilst other streaks would show cocci retaining some of the stain.

The coverslip from the left flank showed no bacteria whatever and only a few leucocytes. That made from the uterine cavity showed a few bacilli of the type of *B. coli*, a few indefinite-looking granules resembling cocci, and some polymorphonuclear leucocytes.

No organisms were found from the smear from the Fallopian tube, only a few leucocytes.

Undoubtedly then, from the above facts, the micrococcus under discussion was none other than *Micrococcus gonorrhoeae*.

In the light of the evidence thus set forth, both clinical and bacteriological, we feel confident in affirming our belief in the case being originally and throughout the disease strictly gonococcal in nature, although at first sight results may not seemingly substantiate our claim, because of the utter failure to identify the gonococcus either by culture or on coverslip at the time of operation, the isolation of *Staphylococcus cereus albus* at the same time, and the finding of *B. coli* in the peritoneal cavity, post-mortem, in conjunction with *Micrococcus gonorrhoeae*. Nevertheless, we feel convinced that a slight consideration of some facts will suffice to dispose of such seeming adverse conditions.

In the first place it is very important to note the absence of any other pathogenic bacterium either at the time of operation, or post-mortem.

Secondly, the patient had been ill eight days previous to entering the hospital, and at operation it was readily seen upon opening the abdomen that the process was one of long duration, the conditions being more pronounced in the splenic

and hepatic regions of the abdomen than elsewhere, hence, it is eminently reasonable to suppose that in this phase the gonococci were dying out in some portions of the exudate and positively dead and gone in others, as was actually borne out by coverslip preparations and cultures at the operation, and by coverslips post-mortem from the exudate in the left flank. Again, the presence of *Staphylococcus cereus albus*, an utterly harmless saprophyte, can be of no moment as it was very evidently present in exceedingly few numbers, being found in one location only, and the rôle it played was that of an insignificant and late secondary invader. The part taken by *B. coli* could have been none other than that of a post-mortem migrant, otherwise, if it were an important etiologic factor, why was it not demonstrable ante-mortem?

Finally, in the presence of a general systemic distribution of *Streptococcus pyogenes*, as shown by post-mortem results, it is worthy of note that there was entire absence of that microorganism in the peritoneal exudate, so far as careful inquiry could establish.

The fatal termination of the case, we are inclined to believe, was largely due to a sudden systemic invasion of *Streptococcus pyogenes* originating possibly from the foci of bronchopneumonia in the right lung, although we cannot neglect a previously existing toxemia, a lowered resistance, and the youth of the patient as prominent factors in encompassing the end.

In addition to the case just reported in full, we wish to report briefly six cases which have come under our observation in the Johns Hopkins Hospital. Our thanks are due the operators for the privilege of reporting these cases.

#### CASE II.—Nos. 7546 and 7668.

Mrs. M. A. Age 25. Admission to the service of Dr. Kelly February 1, 1900, complaining of abdominal pain and tenderness, nausea and vomiting, and constipation.

Married 8 weeks. Menstrual history normal until marriage. Since marriage first two periods normal, but the last period still active; began a little before time and has been associated with severe pain which confined the patient to bed. She has been in bed one week suffering from pain in the abdomen and dysmenorrhea. Five days ago she was seized with very severe pain in the lower abdomen, especially marked in the right iliac region, causing her to place her right thigh in flexed position, where it is at present. Two days ago the abdominal pain became more acute and nausea and vomiting began. She has had no chills.

On admission the abdomen was distended and very tender throughout. No especial points of tenderness. No dullness on percussion. The tongue was coated and the patient appeared very dull and apathetic. The leucocytes were 13,000.

Doctor Kelly operated the next day, removing both uterine tubes. On opening the abdominal cavity about 300 cc. of slightly turbid, viscid fluid escaped. The bowels were distended and tympanitic, everywhere covered by a fibrinous lymph deposit. The omentum was shrunken and intensely injected. Both tubes were straight, deeply injected, adherent to the intestines and pelvic walls. The left tube had a constriction at its fimbriated end, but on pressure a thick yellow pus exuded. Cover-glass preparations showed no organisms. Cultures were not taken.

The abdomen was washed out with a liter of salt solution and closed without drainage. The patient was discharged after 27 days.

In the meantime, she had several attacks of severe abdominal pain, one on the 19th day being particularly severe. There was no nausea and vomiting; the abdomen was not tender.

After being home about two weeks the patient had another

severe attack of general abdominal pain associated with nausea, vomiting, abdominal tenderness and distention, and marked constipation. The attack lasted about three days and then became gradually better.

The patient was admitted for the second time on March 23, 1900, and an exploratory celiotomy was done on March 24, when various evidences of the past peritonitis were found. The omentum was still thickened and inflamed, attached to the abdominal wound, and at one point also to a loop of small intestine in such a manner as to cause an acute kink. There were a few adhesions of fibrin over the intestines and some areas of injection. The omentum was detached from the knuckle of gut, its bleeding end ligated, and the abdomen was filled with salt solution and closed with interrupted silk-worm gut sutures.

The patient made an uneventful recovery and was heard from in January, 1902. She had been perfectly well in the meantime, having menstruated but once, immediately after the first operation.

#### CASE III.—Gyn. No. 7670.

Miss N. G. (colored). Age 20. Admitted March 23, 1900.

The patient was admitted to Doctor Osler's service on March 22, complaining of pain in the abdomen.

Menstrual history normal, until two months ago. Slight leucorrhea. The patient was not married, but had a normal child-birth in June, 1899. The present illness began February 15, after exposure to wet. The next morning patient had cramps in lower abdomen. She was confined to bed for six days with pain. She had no chills, nausea, nor vomiting. She was then up and about the house, but still feeling ill until March 1, when pain in the right inguinal again drove the patient to bed, where she has remained since. She has vomited on two occasions after eating. The bowels have been no more constipated than before present illness. For the past two days there has been a whitish vaginal discharge.

On admission the abdomen was distended and tympanitic, showing fairly distinct intestinal patterns about the umbilicus. The abdomen was soft on palpation and was not particularly tender, except about the umbilicus.

The temperature on admission was 101.2°. The patient had three fluid stools the day of admission. Her leucocytes were 19,000.

Vaginal examination revealed a retroflexed, adherent uterus and some induration on the left side.

*Operation* March 23. Dr. Miller. The peritoneum and intestines were much injected and showed a fine fibrinous deposit, with here and there large flakes of white material. The omentum was markedly injected and adherent at one point to a coil of small intestine. The vermiform appendix was injected, coiled on itself, and covered with fibrin. The uterus, tubes, and ovaries lay in the cul-de-sac of Douglas and were completely covered by fresh fibrinous adhesions to the intestines. On separating the adhesions and bringing the pelvic structures into view, a white pus exuded from the open ends of both tubes. The tubes were removed, the abdominal cavity was irrigated several times with normal saline solution, and a considerable quantity of this solution was left in the cavity. The abdomen was closed with interrupted silkworm gut sutures. No bacteriological report.

After the operation the patient complained of severe abdominal and pelvic pain for about four days. The intestines, however, were never greatly distended, and a free movement of the bowels was obtained on the fourth and fifth days. The highest temperature of 102.2° occurred on the fourth day. Her temperature became normal on the eleventh day and she was discharged well on the 22d day.

#### CASE IV.—Gyn. Nos. 9149 and 9223. J. W. Colored. Age 19.

Patient first admitted to the service of Dr. Kelly, October 22, 1901, complaining of pain in the lower abdomen, and in the back, of a bearing-down character. She was examined under ether and a curettement was done. Nothing abnormal could be found in the pelvic organs except a bilateral cervical tear which dated from the birth of a child 16 months previously. During a week in the hospital she had no elevation of temperature, no leucocytosis, and the urine was normal.

She was readmitted Nov. 15 with the same symptoms. While under observation for a week the temperature reached 100° F. on two days. On Nov. 21 the cervix and perineum were repaired, no disease of the adnexa being discovered. On the second day after operation her temperature reached 102° F. but became normal on the third day. The patient complained of so much pelvic pain that the interne made an examination on the morning of the nineteenth day after operation and found an extremely tender mass to the left of the uterus. At 4 p. m. of the same day her temperature was 102° F. and at 5 p. m. 103°. She complained of severe general abdominal pain, and there was some distention. The temperature reached normal the next morning (Dec. 11) and remained normal until her operation, Dec. 12.

*Operation:* Dr. Russell. A tuboovarian abscess on the left and an open tube on the right discharging pus into the pelvis, where a considerable quantity of free pus was found. The intestines lying in the pelvis were congested and covered by a fibrinopurulent exudate. Throughout the peritoneal cavity there was a fibrinopurulent exudate of low grade. A hysterosalpingophorectomy was performed and the abdomen was closed without drainage. Pus from tubes and peritoneum showed gonococci. Cultures were negative. An otherwise normal convalescence was interrupted by a left-sided pleurisy lasting from the 8th to the 14th day.

This case is atypical because of the mild character of her peritoneal invasion which had undoubtedly spent its force after 24 hours and before the operation was undertaken.

#### CASE V.—Surgical No. 12,759.

Miss E. M. Age 19.

Admitted to the service of Dr. Halsted December 5, 1901, complaining of severe abdominal pain of four days duration. The pain was more severe in lower abdomen on the right side. She had fever, some nausea, no vomiting, no chills. Burning micturition. Patient has had a vaginal discharge for two weeks. The present illness began during the menstrual period.

*Physical Examination:*—The abdomen is not distended. There is some fullness in the right side. Respiratory movements are shallow, but present over the whole abdomen. Liver dullness three fingers above costal margin. Percussion note is generally tympanitic, but impaired in right flank. There is some general tenderness and rigidity, but no real muscle spasm, except over the right lower quadrant. Here there is a point of greatest tenderness. Temperature 102.5°, pulse 112, leucocytes 32,400.

The patient was operated upon by Dr. Finney immediately upon admission. Abdominal incision outside of right semilunar, rather low down, as the operator considered the possibility of tubal disease. The peritoneum was reddened and injected. The cecum was first drawn into the wound and the appendix sought. Apparently normal except for serous inflammation.

Patient put in elevated position and the pelvis explored. The intestines of the pelvis covered by flakes of fibrin and a small quantity of thin yellow pus. Tubes both enlarged, friable, extremities extremely red and swollen, and yellow pus was exuding from both extremities. Both tubes were removed

and the pelvis washed out with salt solution. The entire peritoneum, both parietal and visceral, was injected and covered here and there with flakes of fibrin. Coverslips made from pus in the abdominal cavity showed abundant diplococci decolorizing by Gram's method. Cultures attempted by dropping a section of Fallopian tube in bouillon were negative.

The patient made an uneventful recovery, the temperature reaching normal on the second day.

CASE VI.—Surgical No. 12,793. S. M. (colored). Age 14. Admitted to the service of Dr. Halsted December 14, 1901, complaining of pain in the abdomen. She began to menstruate at eleven and had no pain until four months ago, since when there has been pain with each period, the periods lasting three to four days. Denies possibility of venereal infection. Four days ago the patient had just finished menstruating and was taken suddenly with abdominal pain in the hypogastrium and throughout the left side. The pain was dull in character with severe paroxysms at intervals, causing the patient to scream. Patient has vomited once each day since the first attack except to-day. Bowels have not moved since the onset, although she had cathartic.

On examination the patient looks dull, the tongue is thickly coated, pulse 100, temperature 101.2°, leucocytes 22,000. Abdominal respiratory movements are practically absent. Abdomen is everywhere tympanitic. There is no dullness in the flanks. The lower half seems distended; liver dullness 6 cm. above costal margin in mammary line. The left rectus is more rigid than right. The entire left side is quite rigid. The lower right quadrant is tender and rigid. During the examination the patient complained of severe attack of pain, and an indefinite wave of peristalsis could be seen in the left side.

The patient was operated upon by Doctor Mitchell immediately after admission. Incision through the left rectus muscle, low down. The intestines were quite firmly adherent and covered by a dry, fibrinous deposit. The inflammatory condition extended to every part of the abdomen, but there were no collections of pus. The appendix apparently normal. Much dirty looking fibrin in region of tubes. Both tubes acutely inflamed and swollen, but there was comparatively little thickening. A very small quantity of pus squeezed from the right tube. The tubes were removed. The abdomen was flushed with a warm salt solution. The fibrin was removed from the intestines of the pelvis, and the abdomen was closed with a small quantity of normal saline solution. Abdominal wall closed in layers.

The patient returned to ward at 10 p. m. in a condition of shock, with a very small pulse of 140. After an enema of hot coffee and salt solution and hypodermics of strychnia, patient had a profuse sweat and rallied somewhat. A salt solution infusion of 800 cc. given at 5 a. m. After twelve hours an enema was given, resulting in the passage of much flatus and some feces. The patient then seemed to do well for two days, when the temperature began to rise rapidly, reaching 105.2° on the fourth day and 106.2° on the fifth day; the patient dying on the sixth day with a temperature of 105.5°. The symptoms were not particularly abdominal.

December 18, the fifth day after operation, blood cultures were taken from the vein of the arm and from these diplococci were grown which were decolorized by Gram's method and would not grow when transferred to ordinary media.

Anatomical diagnosis at autopsy: Acute fibrinous peritonitis; acute vaginitis and endometritis, bronchial pneumonia, hyperplasia of mesenteric lymph-glands.

Cover-slips and cultures taken at the operation from the pus in Douglas pouch were negative.

CASE VII.—Surgical No. 13,053. K. S. Age 5½ years.

Admitted to the service of Dr. Halsted Feb. 21, 1902, complaining of abdominal pain; vomiting, frequent and burning micturition. The frequency of micturition had existed two weeks, the burning five days, and the severe abdominal pain 24 hours.

*Examination:*—The child lay on the right side with her legs flexed. Extension of the thighs caused pain. Abdomen not distended; respiratory movements absent in lower half of abdomen; no fullness in fossae or flanks; abdomen everywhere tender and rigid, but no muscle spasm; tenderness most marked in the left flank and right iliac fossa; percussion tympany everywhere over abdomen. Pulse 160, temperature 100°; leucocytes 25,500. From a profuse creamy vaginal discharge typical gonococci were demonstrated in abundance.

*Operation:*—Dr. Mitchell, double salpingectomy, pelvis wiped and flushed, closure without drainage—recovery. A small quantity of free creamy material found on opening the abdomen. The peritoneal coats reddened, and many subperitoneal hemorrhages present. Pelvis contained much free pus. Both tubes were swollen, injected, and yielded pus when squeezed. From pus in the pelvic peritoneal cavity gonococci were grown on hydrocele agar.

After Cushing's excellent paper and v. Brunn's more recent and very exhaustive review of the literature, it would be useless to abstract again all the cases reported. It may be of value, however, to make an analysis of the cases, classifying them on the grounds of bacteriologic evidence, and then to study them with reference to prognosis and treatment. We have omitted Sanger's two cases reported by v. Brunn. The evidence of general peritonitis is not conclusive, and Sanger reports them as cases of pyosalpinx with extensive pelveoperitonitis. In addition to the 28 cases reported by Cushing and by v. Brunn, we have been able to add our 7, above reported, and 7 cases from the literature, reported by Frank, Doederlein (3 cases), Wilisch, Dowd, and Frank and Koehler.

These two tables show a total of 39 cases of general peritonitis due to infection by the gonococcus. Manifestly this is too small a number from which to draw conclusions as to prognosis and treatment. A recovery list of 69 per cent would indicate a good prognosis in this disease as compared with general peritonitis considered in all its etiologic forms.

If we adhere to figures, we see a decided advantage in the operative treatment—79 per cent of the operative cases having recovered, against 53 per cent of recoveries among those not operated upon. But a close study of individual cases demonstrates the fact that numerical statistics may not truly represent the merits of two different methods of treatment.

Of the 18 cases in the first table, 13 were operated upon for peritonitis, 11 of these recovering. The 5 cases not operated upon died. A careful scrutiny of these 5 cases shows the probable futility of any form of treatment after the diagnosis of general peritonitis had been made. In Frank's case general peritonitis quickly followed an operation for the removal of pus tubes, irrigation and drainage being used. The patient died in 72 hours with fulminating peritonitis. Mejia's case, a child 5 years old, entered the hospital moribund after abdominal symptoms of 8 days' duration. Von

TABLE OF CASES IN WHICH THERE WAS BACTERIOLOGIC PROOF.

Year.	Author.	Age of patient.	EVIDENCE.				Result.
			Obtained at	Culture and Cover-glass.	Cultures only.	Cover-glass only.	
1895.....	Frank.....	17.....	Autopsy.....	..	..	+	Death.
1896.....	Sutton.....	18.....	Operation.....	..	..	+	Recovery.
1897.....	Mejia.....	5.....	Autopsy.....	+	..	..	Death.
1899.....	Cushing.....	25.....	Operation.....	..	..	+	Recovery.
1899.....	do.....	18.....	do.....	+	..	..	Recovery.
1899.....	Doederlein.....	3 adults	do.....	..	..	+	Recovery.
1899.....	V. Leyden.....	29.....	Autopsy.....	+	..	..	Death.
1899.....	Muscatello.....	48.....	Operation.....	+	..	..	Death.
1900.....	Metzner.....	28.....	Autopsy.....	..	..	+	Death.
1901.....	Willisch.....	adult.	Operation.....	Bacteriologic research showed gonococci.			Recovery.
1902.....	Dowd.....	7.....	do.....	..	..	+	Recovery.
1902.....	Frank & Koehler.....	adult.	Autopsy.....	..	..	+	Death.
1902.....	Authors' Case I.....	10.....	Operation and Autopsy.....	+	..	..	Death.
	do Case IV.....	19.....	Operation.....	..	..	+	Recovery.
	do Case V.....	19.....	do.....	..	..	+	Recovery.
	do Case VII.....	5½.....	do.....	..	+	..	Recovery.

Remarks: 18 cases { Operated upon... 13 { Recovery, 11  
 { Not operated upon 5 { Deaths, 2  
 { Deaths, 5

TABLE OF CASES WITH CLINICAL EVIDENCE ONLY.

Year.	Author.	Age of patient.	EVIDENCE.		
			Obtained at.	Character of.	Result.
1887....	Ceppi.....	26....	Bedside, pelvic puncture....	Gonorrhea, severe peritonitis symptoms. Puncture of pelvic abscess and gonococci microscopically.	Recovery.
1890....	Penrose.....	adult	Operation.....	History, pyosalpinx and general peritonitis. Operation. Cocci in pus from tube not identified.	Recovery.
1890....	Huber.....	7....	do.....	Vaginitis, sudden symptoms general peritonitis. Operation. Sero-purulent exudate. No bacteriologic research.	Death.
1890....	Thirolaix.....	19....	Bedside and autopsy.....	Cervical catarrh, double pyosalpinx, general peritonitis. Death. General peritonitis developed after treatment in hospital 3 weeks. Death in 26 hours.	Death.
1893....	Menge.....	adult	Operation.....	Manipulation of pus tubes followed by general peritonitis. Gonococci in culture from tubes.	Recovery.
1893....	Veit.....	5 adults.	Bedside.....	Gonorrheal infection just before or during puerperium. Symptoms of general peritonitis. Symptomatic treatment. Chronic gonorrheal pyosalpinx followed.	Recovery.
1894....	Chaput.....	17....	Operation.....	Symptoms of general peritonitis. Celiotomy, salpingoophorectomy. Second celiotomy 5 days later. "Paralysis of intestine."	Death.
1895....	Menge.....	2 adults.	do.....	General peritonitis following, in one case an acute pyosalpinx, and in one case rupture of a pus tube. Bacteriologic research negative.	Recovery.
1896....	Bröse.....	2 "	Bedside.....	General peritonitis following, in one case manipulation of a gonorrheal pyosalpinx, and in one case, spontaneous rupture of a pus tube.	Recovery.
1896....	Baginsky.....	12....	Bedside and autopsy.....	Vulvovaginitis of mixed infection, gonococci and staphylococci. General peritonitis. Death. Autopsy, ovarian abscesses, purulent peritonitis. No bacteriology.	Death.
1897....	Körte.....	adult	Operation.....	Rupture of a pyosalpinx, collapse and gen'l peritoneal symptoms; operation, intracellular diplococci in abdominal exudate. Not surely gonococci.	Recovery.
1898....	Braquehay.....	4½....	Bedside and operation.....	Gonorrheal vulvovaginitis, symptoms of general peritonitis. Operation. Fibrinous exudate, recovery with recurrent joint inflammations. No bacteriology.	Recovery.
1902....	Authors Case II.....	25....	Operation.....	Onset of general peritonitis during menstruation 8 weeks after marriage. Operation. Double pus tubes, general fibrinopurulent peritonitis. Bacteriology negative.	Recovery.
	do Case III.....	20....	do.....	Leucorrhœa of recent origin. History of peritoneal inflammation. Operation. Double pus tubes. General fibrinous peritonitis. No bacteriology.	Recovery.
	do Case VI.....	14....	Operation and autopsy.....	General peritoneal symptoms just after menstrual period. Operation. Pus tubes, fibrinous peritonitis. Death. Antemortem blood culture showed gonococcus septicæmia.	Death.

Remarks: 21 cases { Operated upon... 11 { Recovery, 8  
 { Deaths, 3  
 { Not operated upon 10 { Recovery, 8  
 { Deaths, 2

Totals; 39 cases { Operated upon 24 { Recovery, 19  
 { Deaths, 5  
 { Not operated upon 15 { Recovery, 8  
 { Deaths, 7

Leyden's patient had been under observation for several weeks because of an ascites due to cirrhosis of the liver. The peritonitis developed insidiously and the diagnosis was made at autopsy. Metzner fails to give a clinical history, but his patient died soon after entering the hospital. Frank and Koehler's case had been very ill for a week, and when first seen "was in no condition to operate upon." Under the expectant plan of treatment she began to improve, but six days later she showed symptoms of metastatic septic emboli and died on the seventeenth day of her acute illness.

The two cases which died after operation were of the hopeless class before an operation was undertaken, and therefore do not militate against this form of treatment. Our case, considering the symptoms immediately before operation, and the post-mortem findings, was presumably one of general streptococcus septicemia. Muscatello performed a vaginal puncture for a localized pelvic abscess and flushed the pelvic cavity with sterile water. Symptoms of general peritonitis followed almost immediately, and celiotomy was not performed for 48 hours, the patient dying the same night. On reading the account of his case it seems not unlikely that a quantity of infectious material was washed into the general cavity at the time of vaginal puncture, and the attempt to cleanse the peritoneum was undertaken too late.

An analysis of the second table shows 11 cases treated by the operative, and 10 by the non-operative plan, with results about equally good. Of the 11 operative cases, 3 ended fatally. Huber's 7-year-old child was first seen with a vulvovaginal discharge, but did not seem to be very ill. She was suddenly seized with collapse and subnormal temperature. The next day her temperature was 100° F., and there was pain in the right iliac fossa and vomiting. She was operated upon and a seropurulent fluid was found. The appendix was normal, but the right tube was inflamed and thickened. Death occurred in 20 hours.

One cannot read the account of Chaput's case without speculating upon the results had non-interference been the plan of treatment. The case was diagnosed one of general peritonitis, probably due to perforation. After opening the abdomen and finding a normal appendix, the entire intestinal tract was investigated for a perforation. Finally the tubes were found distended with pus and removed. Failing to get the bowels moved, another celiotomy was done on the fifth day, and three days later the patient died from "paralysis of the intestines."

Mitchell's first case (Author's Case VI) suffered extreme shock from the operation. She rallied, however, and apparently did well until the fourth day, when she suddenly became profoundly ill and her temperature reached 105.2°. On the fifth day her temperature reached 106.2°, and a blood culture taken on this day yielded a pure growth of gonococcus. She died on the sixth day.

Of the 10 cases treated symptomatically, those of Thiroloix and Baginsky died. In Thiroloix's case the symptoms of peritonitis developed after three weeks' hospital treatment for double pyosalpinx, and she died 26 hours later. The

autopsy revealed a fibrinous peritonitis, there being "not a drop of serous or purulent fluid in the peritoneal cavity." In view of such a sudden death while under hospital care, one questions whether some other agency was not at work with the general peritonitis. It is at least highly probable that an operation would have availed nothing with this condition of the peritoneal cavity. Baginsky's case, a child of 12 years, was admitted with a vulvovaginitis; and, from the beginning, showed rather severe peritoneal symptoms. Nothing is said as to the length of time these symptoms had been present or how long the child was under observation before dying with "frightful pain, loud crying, failure of the pulse, vomiting and heart collapse."

While the above record of 19 recoveries in 24 operative cases is a most excellent showing, we can find nothing in the analysis of the seven cases which died without operation to indicate that an operation would have saved any one of them. We might, for the sake of argument, except Baginsky's case; but the records in his case are too meagre to warrant valuable conclusions. On the other hand, as we have pointed out, operation may have determined the death of Chaput's case.

How many of the 19 recoveries were due to the operation is a matter of mere speculation without scientific value.

But we have the positive list of 8 recoveries out of 15 cases not operated upon. These cases were all carefully observed and there is practically no doubt about the diagnosis. As we have seen, 7 deaths in this list were due to conditions which no form of treatment would have overcome, unless we except the one case of Baginsky.

To study the cases reported by Veit and by Bröse, which were carefully observed throughout their illness, one is forced to admire the courage required for a course of "masterly inactivity" in the face of such symptoms. It is characteristic of these gonococcus victims to be extremely ill, and it requires courage for the surgeon to lay aside the means which so often present the only hope in other forms of peritonitis, and await developments under the expectant plan of treatment.

Our observations in the wards of the Johns Hopkins Hospital embrace a series of 9 cases of general peritonitis due to the gonococcus. The experience thus gained, together with a study of the literature, convinces us that surgical measures in gonorrheal peritonitis are of doubtful therapeutic value.

However, the question of differential diagnosis will always need careful consideration, and where there is a reasonable doubt, operation should be performed. The practitioner who does not see many cases of general peritonitis should not treat any suspected case of peritonitis on the expectant plan without sharing the responsibility with one who does a great deal of abdominal work and is thoroughly competent to make a diagnosis.

Every surgeon should be so familiar with the symptom complex of appendicitis as to make a reasonably certain diagnosis of general peritonitis arising from that source. The

picture of a general peritonitis arising from a gonorrheal infection is even more characteristic in its preliminary phases. A history of a blennorrhea of recent date or long standing, with the discovery of gonococci in the cervical, vaginal, urethral or glandular secretions, should make the surgeon very suspicious. If with this onset there is a history of pelvic pain and tenderness, and a mass can be made out in one, or preferably in both, ovarian regions, the diagnosis becomes probable. If a general peritonitis accompanies the above conditions and has occurred immediately after the manipulation of pus tubes, or during the menstrual period, or in the puerperium, the diagnosis is almost a matter of certainty.

If, on a question of diagnosis, the peritoneal cavity be entered and a dry, plastic peritonitis, characteristic of gonorrheal infection, be discovered, the intestines should be disturbed as little as possible. There is probably no gain in attempting to wipe off the dry fibrinous deposit, the patient's vitality is greatly reduced when the intestines are insulted, and there is great danger of the loops adhering in malposition and giving rise to intestinal obstruction. (See Chaput's case and our case II.)

If the tubes contain pus in appreciable quantities they should be removed. The question of removal of tubes when there is no accumulation of pus is one to be decided by various circumstances, such as the social conditions of the patient and the desirability of risking a preservation of the child-bearing function against the danger of future trouble from pus tubes. It is well to know that the more progressive gynecologists are beginning to doubt the advisability of operation for gonorrheal pus tubes.<sup>3</sup> We cannot forbear a warning at this point, although it be somewhat irrelevant to the question under discussion. When pus tubes or a pelvic abscess are operated upon by puncture per vaginam, irrigation should never be used. One is never sure that the peritoneum has not been opened, and the abscess can always be as well cleansed by wiping with dry gauze.

The symptoms of an acute gonorrheal peritonitis—abdominal distention, tenderness and rigidity, vomiting, elevation of temperature, and frequency of pulse—are similar to those of other forms of general peritonitis; but the clinical course of the disease is quite characteristic. After a very acute onset and unusually stormy period of from 1 to 3 days, the symptoms suddenly abate, and the patient makes a rapid recovery, usually preserving as a legacy an intraperitoneal exudate, pelvic adhesions, or pus tubes.

It is generally believed that this disease is particularly fatal to children. We believe this to be due not entirely to the susceptibility to infectious diseases characteristic of childhood, but in larger degree to the fact that children fail to receive the treatment accorded to adults. When an adult becomes suddenly ill with abdominal pain, vomiting, and evidence of collapse, the first injunction is absolute rest in bed.

But children do not take kindly to this form of treatment; and, as in our case No. I, they are too often allowed, and even urged, to join their companions at play and to attend school. Consequently their powers of resistance are lowered at a time when every effort should be made to conserve their energy.

In the treatment of a case of general peritonitis due to the gonococcus, we recommend absolute rest in bed, hot turpentine stupes alternating every half-hour with hot water stupes, mild catharsis, liquid diet, cold sponges for the high temperature, and stimulative treatment according to the severity of the symptoms.

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## PERIPHERAL VENOUS THROMBOSIS IN PNEUMONIA, WITH REPORT OF THREE CASES AND A REVIEW OF THOSE PREVIOUSLY RECORDED. ABSTRACT.<sup>1</sup>

BY WALTER R. STEINER, M. D.,

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During the past decade our attention has been especially called to venous thrombosis as occurring in connection with certain infectious diseases and as following some abdominal operations. A considerable number of cases has been reported where venous thrombosis was found in typhoid fever and influenza, but there is slight reference to its being seen in pneumonia.

Da Costa reported his first case in 1894 and considered it unique. Four years later he gave the histories of two more cases and succeeded in finding six previously published. Shortly after this Welch was able to add fourteen more, making the total number of cases twenty-three. But previous to these writers Valette had reported one personal case and had collected three others. Two of his cases, however, were included in Welch's list. Since then a number of additional cases have appeared in the literature. Jones and Hall have both placed one case on record, and recently Gauchet, and Sears and Larrabee have considerably added to the number already existing.

Gauchet made Venous Thrombosis in Pneumonia the sub-

ject of his thesis and gave in abstract twenty-one cases. Some of these should be excluded as they were not typical lobar pneumonias, but due to influenza. I have consequently not added three to my list and have omitted the mention of two more for other reasons. For in one of the latter no *peripheral* venous thrombosis was found, and the other had syphilis and mitral stenosis, so that the thrombosis might have had another origin. There remains, then, only one of Gauchet's cases which I had not already included in my group. Much of the ground traversed by his thesis had already been gone over by me before my attention was called to his work. Sears and Larrabee found ten instances of venous thrombosis in 949 cases of pneumonia treated at the Boston City Hospital. Abstracts of all these recorded cases will be given in our forthcoming article. The following three cases are the only ones that have been met with in a series of about 500 pneumonia cases at the Johns Hopkins Hospital.

CASE I.—*Pneumonia of both lungs; crisis on the ninth day; accompanying pleurisy of both sides; second attack of pneumonia seven days after the crisis, of five days' duration; thrombosis of the right popliteal vein twenty-eight days after the crisis and six days after the termination of the second pneumonic attack; gradual recovery.*

<sup>1</sup> Abstract of a paper read before the Johns Hopkins Hospital Medical Society February 3, 1902. The paper in full will appear in Volume xi, The Johns Hopkins Hospital Reports.

James A., aged 21 (Hospital No. 25,220), was admitted Jan. 9, 1899, complaining of pain in the left side, cough and loss of appetite. There was nothing of moment in his family or past history. Two weeks before his admission he had caught cold and ten days later had a severe shaking chill. A headache, dry hacking cough and an expectoration slightly blood-tinged were his other symptoms. He appeared to be a well-nourished, powerfully built negro. His respirations were a trifle rapid and there was some dilatation of the *alæ nasi*.

In an examination of his thorax the right side seemed to move slightly more than the left. The percussion note was slightly impaired over the upper left side and the breath sounds here were feeble and suppressed in quality. Over the left back the note was also somewhat impaired and the breath sounds had a distant quality—in the interscapular region distant tubular breathing was heard. The examination of the right side was negative save that below the angle of the scapula there was a distinct impairment of the note and marked tubular breathing.

Two days later the pneumonic process seemed to involve the whole left lung and right lower lobe. A pleuropericardial friction rub was heard at the apex of the heart and the pulmonic second was markedly accentuated. There were symptoms of pleurisy at both bases. The crisis seems to have occurred on the ninth day and the lungs were slowly undergoing the process of resolution when, seven days later, there was noted a sudden flare up of temperature, accompanied by a chill and prune juice sputum. No further lung involvement could be detected on examination, but his respirations were somewhat hurried and his *alæ nasi* dilated with each inspiration. His temperature remained elevated for five days. Four days after its fall and twenty-six after his crisis he developed a thrombosis of his right popliteal vein, attended with quite marked edema of his foot and leg. His temperature rose at the onset to 100.8° and he complained of pain in the leg, especially at the calf. Nothing could be felt on palpation. By the application of the lead and opium lotion the pain was relieved and the swelling reduced in size. He was discharged five weeks after its onset, at his urgent request, the swelling having almost disappeared. He was readmitted seven days later complaining of a swollen right leg. In two weeks the swelling went down and he was discharged again. He was advised to apply a tight bandage to the right leg to serve as a mechanical support.

*CASE II.—Right lobar pneumonia; severe infection; thrombosis of the right internal saphenous vein on the sixth day of the disease; death on the twelfth day.*

Oliver L., aged 63 (Hospital No. 33,727), was admitted Feb. 1, 1901, complaining of feeling badly all over and of a dry mouth. His family history was negative. He had had one-sided hemiplegia (side not stated) about forty-three years previously, which left him considerably disabled for a long time. Chancere when thirty-five years old, no secondaries. Several attacks of gonorrhea. Was a heavy drinker. His present illness began ten days before his admission with a

pain in the right side. It was of but short duration. This was accompanied by a cough and slight expectoration, which was never blood-tinged. Two days before coming to the hospital he had a severe shaking chill. He was a fairly well-nourished old man with lips and cheeks slightly cyanotic. His respirations were 38 to the minute, his temperature 101.4° and his pulse 120 to the minute, of good volume, fair tension and regular in force and rhythm. The vessel walls were considerably sclerosed.

In an examination of his thorax the expansion seemed limited, a little less on the right side. The pneumonic involvement included the right upper and middle lobes. The left side was negative. The heart sounds were somewhat feeble and a soft systolic murmur was heard at the apex. The abdomen was negative. Both extremities presented quite marked varicose veins.

Three days later the varicose veins of the right leg began to cause him considerable pain, especially above the knee, where they were slightly red, and quite firm and tender on palpation. His temperature, which had been slowly falling, rose on this day to 102.8°. His lower right lobe now began to show signs of involvement. He grew slowly worse and developed Cheyne-Stokes' breathing. Two days after the onset of the thrombosis it was noted that the right internal saphenous vein was distinctly visible and the size of one's little finger. It was cord-like on palpation. Marked edema of the right foot and lower two-thirds of the leg was also observed. The patient gradually sank. Did not react to saline infusions and died quietly at 6.30 A. M. on the twelfth day of his disease.

At the autopsy, unresolved pneumonia of the right lung was found with compensatory emphysema of the left lung; thrombosis of the right internal saphenous vein; edema of the right leg; fatty metamorphosis of the liver; anemic infarction of the spleen and fragmentation of the myocardium.

*CASE III.—Left lobar pneumonia; severe infection; termination by lysis; thrombosis of the right popliteal vein six days after patient's temperature was normal; gradual recovery.*

Eugene W., aged 27 (Hospital No. 37,464), was admitted Jan. 4, 1902, complaining of pain in the left side and fever. His family history was negative save for some indefinite history of rheumatism. Several years previously he had an attack of what seems to have been rheumatism. Had had pneumonia twice before, the last time being during the past winter. Had had several attacks of gonorrhea. Was a hard drinker. Five days before his entrance into the hospital he "got wet and caught a heavy cold on his chest." The day following he had a slight chill and complained of pain in his left side. Some cough, shortness of breath and rather profuse expectoration were additional symptoms. He had not noticed whether the expectoration was blood-tinged. That night he had fever. Had been quite constipated since the onset of his present illness. He was a very well-nourished, muscular negro. His respirations were labored and shallow, with an occasional expiratory grunt. There was some dilata-

tion of the *alæ nasi* and some cyanosis. His tongue was dry and coated.

In an examination of his thorax, the left side looked larger than the right, but the expansion was equal. The pneumonic process seemed to involve the lower left lobe. Here the vocal fremitus was absent, the note on percussion was flat and the breathing was tubular. The heart sounds were somewhat indistinct but seemed clear. A pleuropericardial friction rub was heard over the heart. His pulse was small in volume, of low tension, irregular and dichrotic. The vessel wall was distinctly felt.

On the day following he seemed worse. The pulse was very small and irregular. The respirations were shallow and hurried, 72-76 to the minute. The heart sounds were almost inaudible, no sound being heard at the apex. He was infused with 1100 cc. of saline solution, having been infused with 500 cc. the evening before. At the time of his second infusion the pulse could not be counted, but the heart-beats numbered forty-one to the quarter. The lung signs were unchanged, except that the note had cleared up somewhat in the left lower lobe behind but had become more impaired above, in the scapular region, where tubular breathing was heard. A well-marked friction rub was audible below the angle of the scapula and at the left base. There was no delirium. The sputum was small in amount, tenacious, not typically rusty but more blood-streaked. Stained specimens showed pneumococci.

The next morning he seemed decidedly better and the lung showed signs of beginning resolution. He improved rapidly from this time on but the resolution process seemed to be very slow. On Jan. 21 the patient's temperature reached normal for the first time and he seemed to be steadily gaining in strength. Six days later he complained of pain in his right lower leg. On examination an elongated, very tender, cord-like swelling, the size of one's little finger, was found in the popliteal space. It was evidently a thrombosed vein and could be traced from this point down the calf to nearly the lower third of the leg. There was no tenderness over the right femoral vein and no swelling of the lower leg. His temperature rose on this day to 99°. On the next day he complained of pain in the right popliteal space. Slight tenderness was detected here on palpation. The cord-like popliteal vein was well felt. His convalescence was further complicated by the flaring up of an old attack of urethritis which was accompanied by a left epididymitis. He was discharged on March 4 in excellent condition. At this time the popliteal vein was no longer palpable.

The number of cases found recorded is small and conclu-

sions drawn from such a list are of necessity somewhat uncertain. Yet we venture to give the following facts which we have obtained from a study of our three cases and the 38 previously reported.

I. The rarity of thrombosis in pneumonia should be noted. Only 38 cases could be collected. This is a matter of surprise, possibly, for pneumonia is a disease in which the blood is especially rich in the elements that are necessary for clotting.

II. In 27 out of the 32 cases which give fairly full statistics, the thrombosis occurred during convalescence, in 1 it was on the day of the crisis, and in 4 during the course of the disease. It must consequently be generally regarded as a sequela and not as a complication of pneumonia.

III. The lower extremities were always involved. I can find no case reported where there was thrombosis elsewhere except Vulpian's case, where a clot was also formed in the right pulmonary artery. There was a case admitted to the Johns Hopkins Hospital (Hospital No. 21,367), where a thrombosis of the left jugular vein was detected, a day before death, in an old man, aged 84, whose heart's action was feeble, who had quite marked arteriosclerosis, and who presented some doubtful signs of pneumonia. No autopsy was obtainable, so I have not included the case in this group. As in typhoid and other infectious diseases, so here we find the thrombi mostly on the left femoral vein. This was involved alone in 6 cases, the left femoral and internal saphenous in 1, the left internal saphenous in 2, the left external iliac, femoral and internal saphenous in 1, the right femoral in 2, the right and left femoral and left internal saphenous in 1, the right internal saphenous in 2, the right popliteal in 2, both femorals in 4, and the common iliacs at their bifurcation in 1. Adding to these the cases where the extremities but not the veins involved are given, we find the left extremity was alone concerned in 16 cases, the right in 10, and both extremities in 7. The more frequent involvement of the left extremity than the right is attributable, quoting Dr. Welch, to the more difficult return flow from the former in consequence of the greater length and obliquity of the left common iliac vein and its passage beneath the right common iliac artery. It has also been suggested that pressure upon this vein by a distended sigmoid flexure or rectum may likewise contribute to slowing of the blood current upon this side.

Of the 41 cases, death occurred in 9 and 25 recovered, no definite information is given of 7. Eight of those who died had autopsies, and in 5 death was due to pulmonary embolism. The etiology, morbid anatomy, symptoms and treatment will be discussed in our future paper.

## THE JOHNS HOPKINS HOSPITAL BULLETIN.

The Hospital Bulletin contains details of hospital and dispensary practice, abstracts of papers read, and other proceedings of the Medical Society of the Hospital, reports of lectures, and other matters of general interest in connection with the work of the Hospital. It is issued monthly.

Volume XII is now completed. The subscription price is \$1.00 per year. The set of twelve volumes will be sold for \$20.00.

## EOSINOPHILIA IN FILARIASIS.

BY WILLIAM J. CALVERT, M. D., U. S. ARMY.

*(From the Municipal Laboratory, Manila, P. I.)*

This work was suggested by the microscopical examination of tissues removed at autopsy from a plague cadaver, from which the following notes are taken.

CASE I.—Native male Filipino, died of bubonic plague a few hours after entering the plague hospital; autopsy revealed the ordinary lesions of plague.

After removing the intestines a large retroperitoneal tumor lying along the line of the large vessels on the right side was seen. This mass extended from Poupart's ligament to the third lumbar vertebra, varied in width from an eighth of an inch to about four inches, and was in places two inches thick. It extended slightly into the right side of the pelvis; and from the right side of the mass several irregular projections extended into the right retroperitoneal space. The mass was of a deep straw color, semi-translucent, soft and apparently made up of distended sacs. On section a light straw-colored fluid escaped and the punctured sacs collapsed. These spaces did not freely communicate. No direct communication with lymphatic vessels was found. On microscopical examination the fluid showed nothing of note.

All of the right iliac and inguinal lymphatic glands were enlarged. One gland above Poupart's ligament was about three-quarters of an inch by one inch in size. Both spermatic cords and testicles were normal.

Filariasis was thought of at the autopsy, but no worms could be found. A portion of the several organs and the lymphatic glands were fixed in Zenker's fluid for microscopical examination.

In all of the organs numerous eosinophilic leucocytes were found in the capillaries.

In lymph vessels in the areolar tissue about one of the iliac lymphatic glands, sections of an adult filaria were seen in three localities. It is possible for the several sections to represent one worm, but this point could not be determined. The diameters of the lymph vessels were greatly enlarged; and the walls were thickened and infiltrated with small cells. Within the vessel numerous poly-morphonuclear and small leucocytes and detritus were seen. All of the tissues immediately surrounding the lymph vessels were intensely infiltrated with eosinophilic leucocytes. The number of eosinophiles rapidly decreased as the distance from the vessel increased. Some poly-morphonuclear and small cells were mixed in with the eosinophiles. In the periphery of the lymphatic gland numerous eosinophiles were seen in the follicles and lymph sinuses, while in the central portion of the gland very few eosinophiles could be found. In a number of white connective-tissue fibrils in the outer coats of the gland capsule three or four eosinophilic granules, situated in a line parallel with the long axis of the fibre, were seen at

either end of the nuclei. These granules were smaller than those seen in the eosinophiles.

In character the eosinophiles in the connective tissue varied greatly: shape oval or triangular; protoplasm stained irregularly with eosin; nuclei round, oval or poly-morphous, and excentrically placed, very faintly or not at all stained with hematoxylin; number of granules varied from one to many, either scattered throughout the protoplasm or collected about the nuclei, leaving the outer portion of the protoplasm clear. With triple stain, some of the cells stained characteristically, while others took a faint orange tint. Eosinophiles in the lymphatic gland and in capillaries of the various organs stained in the ordinary way with hematoxylin and eosin and triple stain. Doubtless the eosinophiles in the lymphatic gland were being transported by the lymph current from the areolar tissue surrounding the gland to the general circulation.

No traces of trichinosis were observed.

The points of interest in this case are: parent worm near a lymphatic gland; eosinophilic infiltration of the tissues about the worm; tumor in retroperitoneal region; marked increase of eosinophiles in general circulation, shown by eosinophiles in capillaries of the various organs.

The presence of a worm surrounded by eosinophiles, some of which are passing through the involved lymphatic gland to the general circulation, eosinophiles in the various organs, and the absence of an increase of eosinophiles in plague, considered in the light of recent literature on the blood in parasitic disease, point to Eosinophilia in Filariasis.

In order to find a case or cases of filariasis for clinical study and to determine the presence of the disease on the Island of Luzon, from ten to twenty specimens of blood from Filipino prisoners of war were examined each day. In all, four hundred and twenty-six specimens were examined with positive findings in two cases. Both cases were in natives from Albay, a province in Southern Luzon. Later a fourth case was found in a native from a province in Northern Luzon, and a fifth case was reported in Manila, but was not examined.

CASE II.—A. P.; male Filipino; native of Albay; has been in Manila one month. No history of previous illness could be obtained. During past three months patient has had occasional chills and fever. Left iliac glands have been painful two months, and the inguinal one month. Patient is a healthy looking, well-built man.

Examination revealed left conjunctivitis; pulsating veins in neck; old variola scars on arms; few râles and roughened breathing in right lung; heart dulness extended from 2 cm. to right of sternum to 2 cm. left of nipple line; area of pulsa-

tion from third to fifth interspace, sounds booming; liver and spleen normal in size. On the left side, immediately above Poupart's ligament, a painful tumor could be palpated. This tumor was, most probably, enlarged iliac lymphatic glands. One inguinal gland was about three-quarters of an inch by one inch in size and painful. Both spermatic cords and testicles were normal.

Eight embryos were found in specimen of blood taken on April 4, 1901, at 11 o'clock P. M.; on April 6, at 9 A. M., one embryo was found.

Blood counts, on April 6, 9 A. M., were as follows:

Reds 3,866,666; whites 18,760.

L. 10.66%  
L.M. 5.66  
E. 12.33  
P.N. 69  
T. 3 200 counted.

April 17 Noon. Reds 4,700,000; whites 22,000.

L. 9.6%  
L.M. 4  
E. 22.4  
P.N. 61.6  
T. 2.4 200 counted.

On April 18, beginning at 9 A. M., hourly counts of the number of embryos per cc. and leucocytes per cmm. (during day time) and differential white blood counts were made during the following twenty-four hours.<sup>1</sup>

Number of Embryos per cc. of blood.

April 18	9 A. M.	0	April 19	1 A. M.	672
" "	10 " "	0	" "	2 " "	840
" "	11 " "	0	" "	3 " "	672
" "	12 Noon	0	" "	4 " "	672
" "	1 P. M.	0	" "	5 " "	504
" "	2 " "	0	" "	6 " "	504
" "	3 " "	0	" "	7 " "	84
" "	4 " "	0	" "	8 " "	84
" "	5 " "	0	" "	9 " "	84
" "	6 " "	84	" "	10 " "	84
" "	7 " "	252	May 1	10 " "	252
" "	8 " "	504	" "	6 2 P. M.	0
" "	9 " "	672	" "	8 8 A. M.	0
" "	10 " "	840			
" "	11 " "	1176			
" "	12 Midnight	840			

April 18, 9 A. M. Reds 4,720,000, whites 23,000.

L. 12%  
L.M. 4  
E. 20  
P.N. 60  
T. 4 200 counted.

April 18, 10 A. M. Whites 18,000.

L. 12%  
L.M. 4  
E. 17  
P.N. 65  
T. 2 200 counted.

April 18, 11 A. M. Whites 18,666.

L. 9%  
L.M. 3  
E. 20  
P.N. 65  
T. 3

April 18, 12 Noon. Whites 18,500. April 18, 12 Midnight.

L. 11%  
L.M. 6  
E. 21  
P.N. 59  
T. 3 200 counted.

April 18, 1 P. M. Whites 26,666.

L. 10%  
L.M. 4.5  
E. 20  
P.N. 60  
T. 2.5 200 counted.

April 19, 1 A. M.

L. 12%  
L.M. 4  
E. 17  
P.N. 65  
T. 2 200 counted.

April 18, 2 P. M. Whites 24,444.

L. 10%  
L.M. 5  
E. 22  
P.N. 58  
T. 5 200 counted.

April 19, 2 A. M.

L. 10%  
L.M. 3  
E. 21  
P.N. 64  
T. 2 200 counted.

April 18, 3 P. M. Whites 20,000.

L. 11%  
L.M. 4  
E. 21  
P.N. 60  
T. 4 200 counted.

April 19, 3 A. M.

L. 10%  
L.M. 3  
E. 15  
P.N. 69  
T. 3 200 counted.

April 18, 4 P. M. Whites 18,666.

L. 12%  
L.M. 3  
E. 15  
P.N. 67  
T. 3 200 counted.

April 19, 4 A. M.

L. 11.5%  
L.M. 3  
E. 11.5  
P.N. 71  
T. 3 200 counted.

April 18, 5 P. M. Whites 18,000.

L. 11%  
L.M. 5  
E. 16  
P.N. 65  
T. 3 150 counted.

April 19, 5 A. M.

L. 11%  
L.M. 4  
E. 18  
P.N. 64  
T. 3 200 counted.

April 18, 6 P. M. Whites 20,000.

L. 14%  
L.M. 5  
E. 13  
P.N. 63  
T. 5 150 counted.

April 19, 6 A. M.

L. 12.5%  
L.M. 4  
E. 15  
P.N. 65.5  
T. 3 200 counted.

April 18, 7 P. M.

L. 16%  
L.M. 5  
E. 12.5  
P.N. 61.5  
T. 5 150 counted.

April 19, 7 A. M. Whites 18,600.

L. 13.5%  
L.M. 3  
E. 17.5  
P.N. 63  
T. 3 200 counted.

April 18, 8 P. M.

L. 14%  
L.M. 4  
E. 19  
P.N. 60  
T. 3 200 counted.

April 19, 8 A. M. Whites 22,000.

L. 13%  
L.M. 4  
E. 14  
P.N. 65  
T. 4 200 counted.

April 18, 9 P. M.

L. 13%  
L.M. 5  
E. 11  
P.N. 68  
T. 3 150 counted.

April 19, 9 A. M. Whites 18,666.

L. 12%  
L.M. 4  
E. 16  
P.N. 64  
T. 3 200 counted.

April 18, 10 P. M.

L. 13%  
L.M. 5  
E. 15  
P.N. 65  
T. 2 200 counted.

April 19, 10 A. M. { Reds 5,200,000.  
Whites 23,000.

L. 13%  
L.M. 3  
E. DA  
P.N. 68  
T. 2 200 counted.

April 18, 11 P. M.

L. 15%  
L.M. 4  
E. 15  
P.N. 65  
T. 3 200 counted.

May 1, 10 A. M. { Reds 5,200,000.  
Whites 18,000.

L. 16%  
L.M. 4  
E. 18  
P.N. 60  
T. 2 200 counted.

<sup>1</sup> Pratt's method of counting the embryos was used.  
L., Lymphocytes. L.M., Large Mononuclear. E., Eosinophiles.  
P.H., Polymorphonuclear Leucocytes. T., Transitional.

May 6, 2 P. M.	{ Reds 5,160,000. Whites 20,000.	May 8, 8 A. M.	{ Reds 5,200,000. Whites 17,000.
L. 12%		L. 13%	
L.M. 4		L.M. 4	
E. 15		E. 14	
P.N. 66		P.N. 66	
T. 3 200 counted.		T. 3 200 counted.	

Consent of the patient and authority to remove the lymphatic glands were obtained, but the operation could not be done on account of other work, and the prisoner was liberated before the glands could be removed.

CASE III.—M. R.; male Filipino; age 56; native of Albay; well built. Physical examination negative excepting slight enlargement of the right spermatic cord, and small right hydrocele. Right testicle was normal in size and hard. Chills, fever and some headache had occurred at irregular intervals during the past year.

Two embryos were found in specimens of blood taken on April 4, 1901, at 11 o'clock P. M.; in that on April 6, 9 A. M., two.

On April 18, reds numbered 3,620,000, whites 8,000 per cmm.

Differential count:	L. 14%
	L.M. 4.5
	E. 15
	P.N. 64
	T. 2.5

On April 23, beginning at 2 o'clock P. M., hourly counts of the embryos per cc. and leucocytes per cmm. (during day time) and differential counts of the leucocytes were made.

#### Number of embryos per cc.

April 23	2 P. M.	84	April 24	3 A. M.	840
" "	3 "	0	" "	4 "	672
" "	4 "	0	" "	5 "	504
" "	5 "	84	" "	6 "	168
" "	6 "	84	" "	7 "	756
" "	7 "	504	" "	8 "	1002
" "	8 "	588	" "	9 "	336
" "	9 "	1680	" "	10 "	588
" "	10 "	1596	" "	11 "	336
" "	11 "	1512	" "	12 Noon	84
" "	12 "	1428	" "	1 P. M.	0
" 24	1 A. M.	1008	" "	2 "	84
" "	2 "	1008	May 6	8	2 0
			" 8	2 "	0

On April 23, 2 P. M.	Red blood count 3,552,000.	Whites 7,600.	5 P. M.	Whites 6,666.
L. 19%			L. 20%	
L.M. 3.5			L.M. 3	
E. 6.5			E. 7.5	
P.N. 68			P.N. 67	
T. 3 200 counted.			T. 2.5 200 counted.	

3 P. M.	Whites 8,000.	6 P. M.	Whites 13,333.
L. 15%		L. 20%	
L.M. 3.5		L.M. 4	
E. 8		E. 7	
P.N. 70.5		P.N. 66	
T. 3 200 counted.		T. 3 200 counted.	

4 P. M.	Whites 8,000.	7 P. M.	
L. 19.5%		L. 20%	
L.M. 4.5		L.M. 3	
E. 8		E. 7	
P.N. 66		P.N. 68	
T. 2 200 counted.		T. 2 200 counted.	

8 P. M.		8 A. M.	Whites 10,600.
L. 16%		L. 25%	
L.M. 4		L.M. 4	
E. 6.5		E. 8	
P.N. 70		P.N. 60	
T. 3 200 counted.		T. 3 200 counted.	
9 P. M.		9 A. M.	Whites 8,600, triple stain.
L. 23%		L. 15%	
L.M. 3		L.M. 2.5	
E. 6.5		E. 20.5	
P.N. 64.5		P.N. 60.5	
T. 3 200 counted.		T. 1.5 500 counted.	
10 P. M.		9 A. M.	Stained with hematoxylin and eosin.
L. 18%		L. 11%	
L.M. 4		L.M. 3	
E. 7		E. 19	
P.N. 67		P.N. 65	
T. 4 150 counted.		T. 2 200 counted.	
11 P. M.		10 A. M.	Whites 7,000.
L. 22%		L. 16%	
L.M. 4		L.M. 4.5	
E. 7		E. 12.5	
P.N. 64.5		P.N. 65	
T. 2.5 300 counted.		T. 2 200 counted.	
12 P. M.		11 A. M.	Whites 7,600.
L. 21%		L. 15%	
L.M. 3		L.M. 4	
E. 6		E. 15	
P.N. 65		P.N. 64	
T. 2 150 counted.		T. 2 200 counted.	
April 24, 1 A. M.		12 Noon.	Whites 8,000.
L. 22%		L. 16%	
L.M. 5		L.M. 4	
E. 8		E. 12	
P.N. 65		P.N. 66	
T. 2 150 counted.		T. 2 200 counted.	
2 A. M.		1 P. M.	Whites 10,000.
L. 22%		L. 14%	
L.M. 3		L.M. 4	
E. 3		E. 12	
P.N. 65		P.N. 68	
T. 3 200 counted.		T. 2 150 counted.	
3 A. M.		2 P. M.	Whites 8,000.
L. 22%		L. 20%	
L.M. 3		L.M. 4	
E. 6		E. 11	
P.N. 67.5		P.N. 64	
T. 1.5 300 counted.		T. 2 200 counted.	
4 A. M.		May 1, 10 A. M.	{ Reds 3,289,000. Whites 14,000.
L. 19%		L. 16%	
L.M. 3.5		L.M. 5	
E. 8		E. 15	
P.N. 67.5		P.N. 62	
T. 2 200 counted.		T. 2 200 counted.	
5 A. M.		May 6.	Reds 4,200,000. Whites 9,000.
L. 18.5%		L. 26%	
L.M. 4		L.M. 6	
E. 14.5		E. 13	
P.N. 61		P.N. 52	
T. 2 200 counted.		T. 3 200 counted.	
6 A. M.	Whites 8,600.	7 A. M.	Whites 12,000.
L. 19%		L. 22%	
L.M. 3		L.M. 3	
E. 10.5		E. 12.5	
P.N. 64.5		P.N. 60.5	
T. 3 200 counted.		T. 2 200 counted.	
May 8.	2 P. M.	{ Reds 3,500,000. Whites 12,000.	
L. 20%		L. 20%	
L.M. 6		L.M. 6	
E. 12		E. 12	
P.N. 60		P.N. 60	
T. 2 200 counted.		T. 2 200 counted.	

## DESCRIPTION OF CHARTS.

Each horizontal line represents eighty-four (84) embryos and one per centum (1%) of eosinophiles. Each perpendicular line represents one hour of time.

CHART I.—A. P. From 9 A. M. to 5 P. M. no embryos were found; during these hours the eosinophilia in peripheral circulation was greatest; from 5 P. M. to 11 P. M. the number of embryos per ccm. of blood was increasing, while the eosinophilia was decreasing; from 11 P. M. to 8 A. M. the number of embryos per ccm. was decreasing and the eosinophilia increasing. The same condition is seen in chart No. 2.

This phenomena may be explained by the local positive eosinophilic chemotaxis exerted by the embryos in the tissues. When the embryos enter the general circulation this local chemotaxis is removed and the eosinophiles gradually re-enter the general circulation.

CHART I.

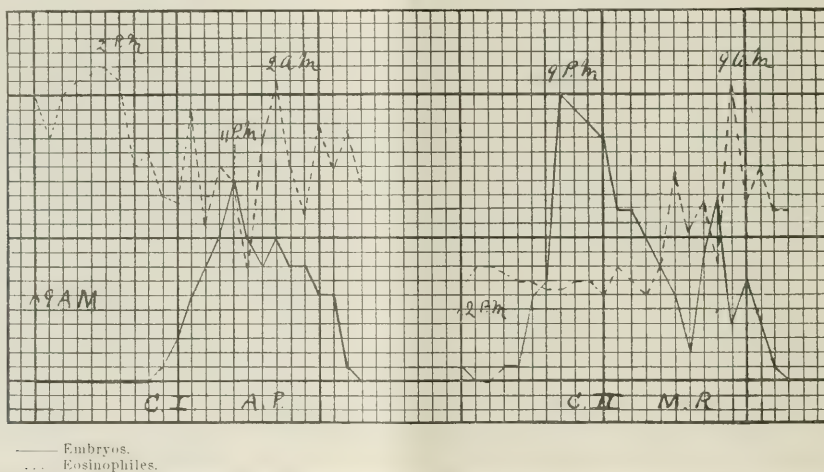


CHART II.

Blood examinations of Case IV substantiate the findings in Cases II and III, but add no new facts. No trichinae could be found in a portion of the biceps muscle.

Cases II and III were recently infected, while in I and IV the duration of the disease could not be ascertained.

Cases I and IV did not have trichinosis, while II and III were not examined.

All of the cases show a decided eosinophilia associated with filariasis. In the most recent case, Case II, the highest eosinophilia was noted.

In cases of long standing an increase of eosinophiles is not found.

These facts lead one to believe that in the early stages of filariasis, leucocytosis with an increase of the eosinophiles may be looked for, and that as the disease progresses, the leucocytosis and increase in eosinophiles gradually decrease to normal.

## BLOOD CULTURES IN PNEUMONIA.

By RUFUS I. COLE, M. D.

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During the session 1900-1901 certain cases of pneumonia in the service of Dr. Osler were studied with the purpose of demonstrating the frequency with which the blood is invaded by pneumococci. The following is a summary of the results obtained.

Cultures were made from the blood in thirty cases, all but one being of acute lobar pneumonia. This exceptional case was one of pneumococcus septicemia, arthritis and meningitis, in which at autopsy the only pulmonary lesion was a very fresh bronchopneumonia, which had undoubtedly developed only as a secondary and terminal event.

In another case there was found at the autopsy only a diffuse bronchopneumonia, but in one lung there was an appearance resembling that of a resolved lobar pneumonia.

The 30 cases from which cultures were made were chosen at random from among the 63 cases studied at the clinic during the session, but the mortality rate of 43 per cent in the series shows that the cultures were made from cases of more than average severity.

The method used was essentially that described in the writer's report on blood cultures in typhoid fever.<sup>1</sup> Eight or ten cubic centimeters of blood were obtained in each case.

As a culture medium in the first cases bouillon was used, five or six tubes of this medium being employed in each case. Later, in order to dilute the blood further and so to overcome the bactericidal effect of the blood, Erlenmeyer flasks, each containing 150 cc. of bouillon, were used, several of these flasks being employed for each culture. It was found, however, that there was some difficulty in readily and quickly determining whether a growth had occurred in this medium, and on account of the suitability of milk as a culture medium for the pneumococcus and the readiness with which the presence and growth of this organism may be recognized by the early acidification and coagulation of the medium, Erlenmeyer flasks, each containing 150 cc. of sterile litmus milk, were used in the later cases. On smears made from this medium capsules may be easily demonstrated, and so a preliminary conclusion can be very quickly and readily reached as to the identity of the infecting organism. In all cases, however, the identity was finally established by its characteristic shape and staining reactions, including the staining of capsules, and by the typical growth in milk and agar, and by the absence of growth, or very slight growth, in gelatin at the ordinary room temperature. In but one of the cases were the cultures contaminated; in a part of the flasks there was a growth of *Staphylococcus pyogenes albus*.

The following table (p. 138) gives a summary of the clinical features together with the time, method and result of the cultures in each case.

Pneumococci grew from the blood of 9 of the cases, 30 per cent, all of which ended fatally. In two of the cases pneumococci were found circulating in the blood three days before death. In the other positive cases the cultures were made a shorter time than this before death, in two of the cases only seven hours. In one of the cases the cultures were negative six days before death, but pneumococci were found three days later.

Thirteen of the thirty cases died, so that pneumococci were not obtained from the blood of four of the cases which ended fatally, notwithstanding the fact that in one case (II) cultures were made on three occasions, 4, 6 and 2 days before death; in another (XV) on two occasions, 4 and 2 days before death; in another (XXIII) on three occasions, 3 days, 1 day and 8 hours before death; and in the other case (XXVII) 24 hours before death. In one of the cases (II) the absence of the organisms in the blood was especially surprising, as thrombosis of the right internal saphenous vein occurred during the course of the disease. But as cultures from this thrombus made both during life and at autopsy proved negative, it is probably to be regarded rather as an example of so-called marantic thrombi than as one of infectious origin, especially as it occurred in an old varicose vein.

Obviously from the results given, cultures from the blood have not been of much aid in diagnosis. In obscure cases of central pneumonia, however, or in cases of general infection unassociated with pulmonary lesions (XVIII), they may be of great value. The greatest value of this procedure clinic-

ally, according to our results, is with reference to prognosis, as was well shown in several cases of the series.

In no other question in bacteriology or pathology have observations been so conflicting as in regard to the frequency of bacterial invasion of the blood during life. This has been largely due, first, to the fact that in many cases the work has been done by clinicians who have not had the requisite bacteriological training; second, to difficulties in obtaining the blood without contamination; and third, to differences in the methods employed. According to the first reports, bacteria very frequently invaded the blood and could often be demonstrated even microscopically in the fresh blood. But by the exercise of greater care it was shown that these observations were faulty, and the contrary view, namely, that invasion of the blood by microorganisms is a rare occurrence, prevailed. However, with improvements in technique, it has been found that in certain conditions, notably typhoid fever, bacteria invade the blood with great frequency. The views in regard to the invasion of the blood by pneumococci have also passed through these successive stages.

The following are the conclusions reached in the more extensive and complete reports published during the past few years:

Sittmann<sup>2</sup> in 1894 was able to demonstrate the organisms in the blood of 6 cases among 16 which he examined. In two of the cases, however, the organisms were only obtained on cover-slips, the cultures being negative, so that in but 4 of 16 cases, or 25 per cent, were the results positive. Three of the four positive cases ended fatally, while of the twelve negative cases, but three died. He used about 5 cc. of blood, making agar plates from this.

Kühnau<sup>3</sup> in 1897, from nine cases of pneumonia, three of which were fatal, obtained the pneumococcus but once in cultures. This case ended fatally. In one other fatal case animal inoculation gave a positive result, though the cultures proved negative. In each case 10 cc. of blood were used and plates were made from this.

In the same year Kohn<sup>4</sup> reports cultures from 32 cases. Twelve of these cases ended fatally, and in seven of these the cultures were positive; while among the twenty cases which recovered, the cultures were positive in but two, making a total of nine positive cases among thirty-two, or 28 per cent. The method employed by Sittmann was used in this case.

The following year Sello<sup>5</sup> reported cultures from 48 cases, pneumococci being obtained in 12, or 25 per cent. Of the negative cases, 27 recovered and 9 died. Of the positive cases, 2 recovered and 10 died.

In 1899, White<sup>6</sup> made cultures from 19 cases, 10 of which were fatal. The cocci were obtained in but 3 cases, all of which ended fatally. The positive results were obtained in one case one day before death, and in the other cases but two days before death, previous cultures made in these cases on the third, fourth and fifth days respectively having proved negative.

In 1900, Silvestrini and Sertoli<sup>7</sup> report finding pneumococci in the blood of 15 out of 16 cases examined. They

TABLE.

Number.	Name.	Admitted, day of disease.	Day of disease.	Hours before death.	BLOOD CULTURES.			CLINICAL FEATURES.		
					No. cc. blood.	Medium.	Result	Recovery or death.	Day of disease.	Remarks.
I.	K.	4	6	24	8	4 Bouillon flasks } 2 Tubes milk.....	Pos.	D	7	Very ill during entire course. Lumbar puncture at time of blood culture.
II.	La.	3 (?)	6	144	8	4 Milk flasks.....	Neg.	D	12	Very ill during entire course. Lumbar puncture on eighth day.
			8	96	8	2 " " ".....				
			10	48	8	3 " " ".....				Thrombosis of internal saphenous vein. Culture from thrombus on tenth day. Result—negative.
III.	Le.	6 (?)	7	7	8	2 Tubes milk..... 1 Tube blood-serum 1 " bouillon.....	Pos.	D	7	Extremely ill on admission.
IV.	Wa.	5	6	..	8	1 Flask bouillon..... 2 Flasks bouillon..... 1 Tube agar..... 1 " hydrocele agar 1 " blood-serum.....	Neg.	R		Case of moderate severity. Temperature fell by lysis beginning on sixth day.
V.	No.	5	6	..	10	2 Flasks bouillon..... 2 Tubes milk.....	Neg.	R		Very ill at time culture was taken. Crisis on eighth day. Post critical rise of temperature.
VI.	S.	4	6	7	8	3 Flasks bouillon..... 2 Tubes milk.....	Pos.	D	6	Very ill at time culture was made. Lumbar puncture made at same time showed presence of pneumococcus meningitis.
VII.	P.	5	6	72	8	3 Flasks bouillon..... 3 Tubes milk..... 1 Tube blood-serum	Pos.	D	9	Quite ill at time of culture but not extremely so. Culture of importance as aid in prognosis.
VIII.	Bu.	2	3	..	8	2 Flasks bouillon..... 1 Flask milk..... 1 Tube milk.....	Neg.	R		Not extremely ill at any time.
			4	..	8	4 Flasks bouillon..... 1 Tube milk.....				
			5	..	8	2 Flasks bouillon..... 2 Tubes milk.....				
IX.	Was.	7	8	..	8	3 Flasks bouillon..... 3 Tubes milk.....	Neg.	R		Not extremely ill. Some delirium. Marked jaundice.
X.	Cole.	6	6	..	8	2 Flasks bouillon..... 2 Tubes milk.....	Neg.	R		Case of moderate severity. Cultures taken during lysis.
			8	..	8	2 Flasks bouillon..... 2 Tubes milk.....				
XI.	Ru.	7	9	..	8	3 Flasks bouillon..... 2 Tubes milk.....	Neg.	R		Very ill on admission. Cultures taken during lysis.
XII.	Re.	2	3	..	8	2 Flasks bouillon..... 2 Tubes milk.....	Neg.	R		Case of moderate severity. Crisis on the fourth day.
XIII.	Wi.	8	12	..	8	2-350 cc. flasks of bouillon.....	Neg.	R		Patient quite sick at time of culture.
XIV.	Wash.	3	7	..	8	3 Flask bouillon.....	Neg.	R		Case of moderate severity.
XV.	Wal.	6	7	96	8	1-300 cc. flasks of bouillon..... 2 Erlenmeyer flasks of bouillon.....	Neg.	D	11	Very ill during entire course.
XVI.	Em.	3	6	48	8	4 Flasks bouillon.....	Pos.	D	6	Patient very ill, high temperature.
XVII.	Ha.	14 (?)	18	24	8	3 Flasks milk..... 2 Flasks bouillon.....	Pos.	D	19	Autopsy showed diffuse bronchopneumonia and an appearance like that of resolved lobar pneumonia in one lung. Patient had persistent hiccoughing before death.
XVIII.	Murray.	(?)	(?)	28	8	3 Flasks bouillon.....	Pos.	D	(?)	Case of arthritis, meningitis and septicemia. Autopsy showed fresh lobular pneumonia, no lobar pneumonia.
XIX.	War.	(?)	6	..	8	3 Flasks bouillon.....	Neg.	R		Patient never very sick during course of disease.
XX.	Co.	5	7	..	8	3 Flasks milk.....	"	R		Not very severe case. Crisis on eighth day.
XXI.	Wi.	5	6	..	8	" " ".....	"	R		Discharged from hospital four days before present admission. This was a second attack. See No. XIII.
XXII.	O'C.	5	6	24	8	" " ".....	Pos.	D	7	Physical signs not absolutely definite. In absence of autopsy cultures were of aid in making the diagnosis certain.
XXIII.	Wa.	6	7	72	8	2 Flasks milk..... 1 Plate agar.....	Neg.	D	10	Extremely sick, high fever, active delirium during entire course of disease.
			9	24	8	2 Flasks milk.....				
			10	8	8	1 Flask milk.....				
XXIV.	Fr.	5	7	..	5	2 Flasks milk.....	Neg.	R		Child 3 years old. Lysis 7-10 days.
XXV.	Ba.	5	9	..	8	4 " " ".....	"	R		Patient not very ill.
XXVI.	V. H.	9	10	..	5	2 " " ".....	"	R		" " " "
XXVII.	Wil.	8	9	24	8	2 " " ".....	Neg.	D	10	Very ill during entire course.
					2 " bouillon.....					
XXVIII.	Wh.	9	10	..	8	4 Flasks milk..... 1 " bouillon.....	Neg.	R		Case of moderate severity.
XXIX.	Ro.	1	3	144	7	3 " " "..... 5 Tubes milk.....	Neg.	D	9	Very ill during entire course. No marked change between the third and sixth days.
XXX.	Fi.	3	5	..	8	6 Flasks milk..... 6 Tubes milk.....	Pos.	R		Rather mild case.

think, however, that the number of pneumococci often, though not always, stands in direct relationship to the severity of the infection.

Within the past year two articles by Prochaska<sup>1</sup> have appeared in which the results of a series of cultures from the blood of pneumonia patients are reported, positive results being obtained in every case. In the first report the results in ten cases are given, and in the second report those obtained in forty additional cases. In 46 of the cases of both series the pneumococcus was obtained in pure culture, in two cases in association with staphylococci and in two cases there was obtained a pure culture of cocci frequently growing in chains, the exact nature of which, whether they were streptococci or a variety of pneumococci, was not accurately determined. Of the 50 cases, 12 died. Positive results were obtained at all stages, in several cases on the second day, in one case two days following the crisis, and in one case three days after the crisis. In the first 10 cases, 4 to 5 cc. of blood were employed, cultures being made in bouillon tubes. In the second series 10 cc. of blood were used. One portion was added to tubes of bouillon, the remainder was poured over agar slants. The most constant results were obtained in the bouillon cultures. The amount of bouillon used, and hence the degree of dilution of the blood, is not stated, and the author does not lay any stress on this factor. He ascribes his good results to the use of large amounts of blood, to the use of bouillon as a culture medium, and to great care in the examination of the cultures.

Our results do not confirm the work of this investigator, notwithstanding the fact that even larger amounts of blood were employed and a much greater dilution was made, and

although the cultures were examined with the greatest care. Doubt will certainly have to be expressed as to the author's views that the number of pneumococci in the blood bears no relationship to the severity of the attack, very mild cases frequently showing very many. My results and those of most other investigators certainly show that the organisms obtained from the more severe and fatal cases are either more numerous or more resistant to unfavorable conditions, for otherwise positive results would not have been obtained only in such cases.

In the report of a very recent meeting of the Verein für innere Medizin in Berlin, A. Fraenkel<sup>2</sup> is quoted as stating that the work of Prochaska had lately been confirmed in his clinic, though he does not state any statistics.

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## MALARIAL FEVER IN INFANCY, PROBABLY MATERNAL IN ORIGIN.

By LINDSAY PETERS, M. D.,

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During my obstetrical service at this Hospital in 1898 one of my patients gave birth to a living child, at term, during a severe malarial paroxysm. A few weeks later the child had developed an anemia of very high grade and malarial organisms were found in its blood. The case was one of considerable interest, but owing to the lack of absolute proof of the intrauterine origin of the infection, at that time I deemed it of insufficient importance to report. Last summer I learned that there were two babies in the lying-in ward born of mothers with malarial infection, but in neither of these cases was especial attention given to the matter of ascertaining whether the child's blood contained malarial parasites at birth. The opportunities for observing these cases occur not infrequently in extensive obstetrical practice

and it has therefore seemed to me important to bring the subject of congenital malarial infection before the Society, to emphasize, if possible, the necessity of more careful notice of such cases in order to settle the disputed question of the transmissibility of the malarial organism from mother to fetus. To show the conflicting views on this subject I will quote some of the authorities: Laveran<sup>3</sup> states that it has been proven in the affirmative beyond a doubt and cites as proof the cases observed by Sue, Hawelka, Duchek, Bein, and Bouzian. The last two, he claims, "establish beyond doubt the existence of congenital paludal fever." On the other hand Marchiafava and Bignami<sup>4</sup> refer to a number of cases in which the blood of fetuses born of women gravely

<sup>3</sup> Laveran. *Traité du Paludisme*. 1898, p. 136.

<sup>4</sup> Marchiafava and Bignami. *Twentieth Century Practice of Medicine*, vol. xix, p. 129.

<sup>1</sup> Read before The Johns Hopkins Hospital Medical Society, February 3, 1902.

ill of malarial fever was examined for parasites with a negative result, and they make the following statement concerning the cases of Bouzian and Bein, cited by Laveran: "We have been unable to find the original report of the first of these cases, but Bein's case is, in our opinion, not above criticism since the presence of malarial germs in the child's blood was noted too long a time after birth and the possibility of post-natal infection could not be definitely excluded." These authors call especial attention to the fact that "no truly demonstrative case of congenital infection has been published since the discovery of the malarial parasites." Furthermore, after a series of autopsies on still-born children of malarious women they express the belief that the fetus enjoys immunity even against the anæmia, parenchymatous degeneration of the liver and other secondary effects of the infection, although these effects may be well marked in the mother. Bastianelli and in fact practically all of the eminent Italian observers agree on this subject with the opinions of Marchiafava and Bignami. Thayer<sup>4</sup> also states that "since the discovery of the parasite no one has been able to bring positive evidence of the congenital presence of parasites in the blood of the new-born child, or of the development of true malarial fever in the infant where the possibility of post-partum infection was out of the question."

These statements show the necessity of further careful work in order to gain positive knowledge on the point under consideration. In view of the well-proven fact that many varieties of bacteria are able to pass from the maternal circulation into that of the fetus, on theoretical grounds at least, one would be inclined to believe the same thing possible for a minute organism possessing the active amœboid motility and penetrating power of the malarial parasite, especially when one considers the thinness of the barrier between the fetal and maternal circulations in the placenta, and, whatever is lacking in the way of positive proof, everyone must admit that there is much to support this idea. The case which I have observed has many suggestive points. Its history is as follows:

The mother was a German woman 27 years of age. She contracted malarial fever in the autumn of 1897 while living on the outskirts of Baltimore. She was treated in the Johns Hopkins Hospital Dispensary for tertian fever and was cured for several months. In the spring of 1898 the paroxysms of chills and fever returned, occurring, as before, every other day. She was then pregnant and on being treated again at the Dispensary the malarial paroxysms disappeared and did not return until the day of her confinement, Aug. 21, 1898. Shortly before the birth of the child she had a severe, shaking chill, followed by fever and sweating. Immediately afterwards uterine contractions began and with only a few severe labor pains the child was expelled before the doctor, who had been summoned, arrived. The above description of the labor was obtained from the patient herself, no attendant having been present during the labor. On the third day of

the puerperium the mother's temperature was reported to be 104° F., following a severe chill. I first saw the patient on that day. She was at that time pale and slightly jaundiced, having an easily palpable spleen and marked herpes on the lower lip. On the following day examination of fresh preparations of her blood demonstrated the presence of typical, half-grown, tertian malarial organisms.

The baby was a well-formed boy, weighing seven pounds. Fresh blood specimens taken from his ear on the second and third days after birth were hastily examined and no organisms were seen. On the third day after birth the infant's axillary temperature was 99° F.

The mother was given quinine immediately after the parasites were found. This treatment was continued daily for several weeks and there was no return of the paroxysms after the first dose of the drug.

On October 10th, the 50th day after her confinement, the mother brought the child to me at the Hospital, stating that the baby had gotten very pale and seemed very sick, refusing to nurse. Examination showed that the child was extremely anæmic, the skin having a faint yellowish tint. The lower border of the spleen could be felt about 3 cm. below the costal margin. Temperature 98.6° F. On the following day, October 11th, a specimen of blood was taken from the baby's ear for examination. The blood was very pale and watery and coagulated very slowly. Unfortunately the percentage of hæmoglobin was not ascertained nor was a blood-count made, but the anæmia was evidently very marked. After searching two fresh, unstained, cover-glass preparations of the blood three malarial parasites of the tertian type were found—one small, extracellular, pigmented form and two half-grown intracellular forms containing light brown, dancing pigment granules. From this time the infant was kept closely under observation in the maternity ward for two days. No noteworthy symptoms were seen and the temperature, taken every two hours per rectum, never exceeded 99.7° F. Quinine was given in the form of a powder—one grain three times a day—and the anæmia and other symptoms disappeared within a few weeks.

Although the mother had never seen the child have a chill, she noticed that since the second week after birth it "got cold and had fevers" from time to time. These symptoms were, no doubt, manifestations of the disease, replacing the ordinary paroxysms observed in adults, for according to Holt,<sup>5</sup> in young children a well-marked chill is rare. In infants it "is replaced by cold hands and feet, blue lips and nails, sometimes slight general cyanosis, pallor, drowsiness and prostration."

The mother also said that she had always noticed that the child was pale, but not enough so to cause her uneasiness until about a week before she brought the child to me, i. e., when it was a little more than five weeks old.

From this history and from the high grade of anæmia it is evident that the infection was not a recent one, hence it

<sup>4</sup>Thayer. *Lectures on the Malarial Fevers*. 1897, p. 95.

<sup>5</sup>Holt. *Diseases of Infancy and Childhood*. 1897, pp. 1077, 1078.

is quite certain that the child either acquired the disease in utero or very soon after birth. Admitting the possibility of the latter explanation of the source of the infection, it nevertheless seems to me that the circumstances of the case are against it, for in the light of recent knowledge the human being cannot acquire malarial fever after birth except through the agency of infected mosquitos of the *Anopheles* variety and the child was born in the third story of a house in a non-malarious locality, only three blocks from this Hospital, where, according to the investigations of Messrs. Hirshberg and Dohme,<sup>6</sup> the likelihood of encountering the *Anopheles* mosquito would be exceedingly small. Moreover, on inquiry, the mother of the child stated that she was never troubled with mosquitos in her room and I did not find any evidence of their presence there. The child could not have acquired the disease in any other locality for it was not taken from the room in which it was born until about a week before being brought to me, i. e., after the disease had already manifested itself. Therefore, in this case, although the possibility of error must be admitted, in my judgment the evidence is in favor of intrauterine infection. If the child acquired the disease after birth it must have been bitten by mosquitos infected by the mother's blood (for there were no other known cases of the disease in the neighborhood), but two other persons living in the same room, the husband and a child of five years, ran the same chance of infection, and yet both remained perfectly healthy.

Both Holt and Rotch<sup>7</sup> agree in the opinion that transmis-

<sup>6</sup> Hirshberg and Dohme. *Distribution of Mosquitos in and about Baltimore*. Read before the Johns Hopkins Hospital Medical Society, December 16, 1901.

<sup>7</sup> Rotch. *Pediatrics*, 1898.

sion of malaria from mother to child in utero is possible and does take place. I trust that more careful observations will positively determine this point.

It may be of some historical interest, in connection with our subject, that in former times, before the discovery of the malarial parasite, cases of malarial fever in infants were reported in which it was supposed that the disease was inherited from the father; in other cases it was held that the child was probably infected by the mother's milk. Some observers also noted cases in which at regular intervals the unborn child had a chill which could be felt by placing the hand on the mother's abdomen. That such cases really occurred is very improbable as it is now known that even after birth a marked chill is rarely seen during infancy and the paroxysms as a rule do not occur at regular intervals as they do in the adult. However, it is quite conceivable that malarial toxins in the mother's blood caused convulsions in the fetus which could be perceived by the mother or the examiner.

I think that the negative evidence furnished by the researches of the Italian observers, whom I have mentioned, loses force when we remember that the failure to find malarial organisms in the child's blood at birth does not necessarily imply that an infection which may not be manifested in the infant for some time after birth was not congenital; indeed it is highly probable that, in the majority of cases in which the infection is transmitted from mother to fetus (assuming that such does take place), the contamination of the child's blood does not occur until labor has begun, when the separation of the placenta affords an opportunity for the mingling of fetal and maternal blood.

## PROCEEDINGS OF SOCIETIES.

### THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

*Monday, December 2, 1901.*

The meeting was called to order by Dr. Hurd.

#### **Catarrhal Otitis Media (non suppurative) as a Factor in the Etiology of Facial Paralysis.** DR. REIK.

(See April BULLETIN, 1902, page 83.)

#### **Exhibition of a Case of Pelvic Tuberculosis.** DR. KELLY.

It is my desire this evening to draw the attention of the Society to a class of cases representing the most difficult of all forms of pelvic suppuration, from the practical standpoint.

It is an interesting fact that for the past 12 years every step marking an advance in the treatment of pelvic abscesses has also marked a step forward in the direction of conservatism, so that now the first plan of treatment thought of is always that of vaginal opening and drainage. In this way the worst cases are often entirely relieved. Sometimes

when after opening the abdomen, I find an inflammatory mass so extensively and densely adherent that its enucleation is a matter of great danger, I then turn to the vaginal route, and make an opening behind the cervix and then continue it on up into the masses until all sacs are opened and free drainage established. While making these manipulations through the vagina, it may be with the help of an assistant, one hand is kept inside the abdomen assisting in the discovery of all foci of suppuration, and protecting the abdominal cavity from invasion from below.

In spite of all these advances in the treatment of pelvic abscesses due to pyogenic cocci, there has been little or no advance made in the treatment of tubercular disease of the pelvic organs. Here a radical operation is always necessary, all the diseased caseous structures must be removed as completely as possible in order to effect a permanent cure. The extent of the operation is only limited by the extent of the disease, which may invade tubes, uterus, ovaries, rectum and bladder.

In the case I am about to report, the disease involved the uterus, tubes and ovaries and the rectum. The operation done to relieve the patient was the removal of the uterus, tubes and ovaries by bisection and removal of a large part of the rectum with proctosigmoid anastomosis.

The patient, Mrs. C., white, aged 34 years, was first examined by Dr. Clark in 1897 and told that she should have an operation for pelvic abscess. She entered the hospital in March, '99, suffering from a very large pelvic abscess. She was very anemic and emaciated, and dated her trouble from the birth of her last child, six years previously.

On opening the abdomen I found such extensive adhesions to the pelvic mass that successful enucleation was deemed impossible in the patient's frail condition. She was placed in the lithotomy position; and, with one hand in the abdomen, a vaginal puncture was performed with the other hand.

She was discharged in six weeks greatly improved in health, but suffered with a slight fecal discharge through the vaginal vault. This discharge persisting, she returned in May, 1900, and I then performed the formidable operation of removing the genital organs and a large portion of the rectum together with all the tuberculous tissue that could be cleaned out of the pelvis. The sigmoidorectal anastomosis was done under great difficulties because of the thickened condition of the rectal stump. Square sutures were used, passing through all coats of the bowel and being tied inside as recently described by Connell of Chicago. The last three sutures were mattress, passed and tied on the outside of the bowel. Both suprapubic and vaginal drainage was instituted.

She was discharged July 6, 1900, much improved in health, but with a fecal sinus again established. For this condition the sinus was curetted several times during the past year. The patient's health continued to improve and she returned November 15, 1901, to show how fat and well she had become. The sinus was completely healed at both ends and bimanual examination showed no evidence of further trouble.

Another case illustrating some of the possible complications following tuberculous disease of the pelvic organs will be presented by Dr. Hunner.

#### **Exhibition of Patient, and Discussion of Dr. Kelly's Case.** DR. HUNNER.

Like the patient Dr. Kelly has just reported, the one I wish to present came to the hospital in a very weak and emaciated condition. She was thirty-one years of age and the mother of ten children. She had always enjoyed good health until the birth of her last child, three years previously. Since that time she had gradually lost weight and strength, and for ten months before admission she had suffered with dysmenorrhea and prolonged and copious hemorrhages. She gave no history of chills or fever. One sister had died of tuberculosis; otherwise the family history was negative. On physical examination, there was no evidence of lung tuberculosis. The pelvis was the seat of a bilateral inflammatory

miss.

Dr. Kelly operated December 5, 1901, removing a tuber-

culous uterus and large lateral masses, by the method of bisection, the cervix being left. At this time there was a general tuberculous peritonitis.

The patient did not do well after the operation, and on December 11, her temperature rose to 104°—the leucocyte count was 30,000. She was examined under nitrous oxide gas and the cervical stump was dilated, a large quantity of foul-smelling pus being evacuated. Again, on December 19, she was taken to the operating-room and the cervix was dilated. A diagnosis was made of a fluid mass in the sigmoid region, and on attempting to reach this by the inguinal route the sigmoid was injured.

The patient improved slowly, and on January 14, 1901, she was allowed to go home, as she did not wish the sigmoidal sinus closed.

She returned in April, very much improved in health. The sigmoidal sinus was still open, and in addition there was a fecal discharge through the vagina. This vaginal discharge began, she said, at the time she left the hospital. Microscopic examination of the granulation tissue about the inguinal wound showed tuberculosis.

On May 1, 1901, I operated, first cutting out the diseased skin and muscle forming the walls of the inguinal fistulous tract. On resecting the disease from the sigmoidal wall, it was found that a lateral closure of the bowel would result in too much constriction. Therefore, about 8 cm. of the sigmoid was resected and an end-to-end anastomosis was effected.

The disease had caused several lateral adhesions of loops of the ileum. At one of these points of adhesion there was a large tuberculous nodule over one centimeter in diameter. This was excised and the resulting bowel openings were closed with silk mattress sutures.

The patient's condition did not warrant an investigation and repair of the enterocervical fistula at this time.

The inguinal wound was closed except at the upper end, where a small strip of iodoform gauze was carried down to the site of anastomosis.

The patient made a rapid recovery. The inguinal wound had entirely closed in two weeks. She refused to have the enterocervical fistula closed, and still had a slight discharge from the vagina when she went home on the 3d of June.

#### **Exhibition of a Surgical Case.** DR. FOLLIS.

This patient, a man aged 24, was admitted to the accident department of the hospital September 8, 1901.

He had been stabbed in the left side of the abdomen two hours previously. This time had been spent in a wagon on his way to the hospital.

On admission the patient was markedly shocked; the pulse could be felt but could not be counted. The transverse, ascending and descending colon, the stomach, and practically all of the small intestine protruded from a wound 13 cm. long, which had divided the left rectus muscle just above the level of the umbilicus. The protruding abdominal viscera were covered with a horse blanket. There was also an

incised wound of the stomach 3 cm. long, from which quantities of food were pouring. After washing off the bowels, an attempt was made to reduce them to the peritoneal cavity, but this was so painful that primary ether anesthesia was induced. The patient's condition was so critical that time was not taken to suture the wound of the stomach; it was clamped and the clamp was left in place. The bowels were retained in the peritoneal cavity by gauze packing. The patient's general condition improved markedly after morphia and stimulation had been given. For the first 24 hours the patient improved steadily, but on the third day he had considerable abdominal pain and vomiting. Suspecting that an obstruction might be present, he was again etherized and the wound explored. An obstruction was found due to the gauze packing. The obstruction was relieved, the clamp was removed from the wound of the stomach, which was then sutured with catgut, and the wound was repacked. The stomach suture did not hold and the patient developed a gastric fistula on the seventh day following the second operation. This fistula closed spontaneously on the seventeenth day. Four weeks after the second operation the patient again showed signs of obstruction and an exploratory incision was made through the right rectus muscle, and an obstruction due to adhesions was found and relieved. Since that time the patient has made a good recovery and is now ready to leave the hospital.

**Demonstration of the Central Nervous System by Means of Clay Models.** DR. A. P. HERRING.

(See April BULLETIN, 1902, page 85.)

**A Laboratory Method of Teaching Osteology.** DR. SIDNEY M. CONE.

Dr. Cone demonstrated a method of modeling the bones of the skeleton in clay, which in his experience has proven of great service to the students, as in this manner they acquire ideas of the size, shape and relation of bones, which could not otherwise be secured.

*Monday, December 16, 1901.*

The meeting was called to order by Dr. Thayer.

**A New Method of Pyloroplasty.** DR. FINNEY.

(To be published later.)

**Pneumococcus Septicemia, Meningitis and Arthritis.** DR. COLT.

During the session 1900-1901 the cases of pneumonia treated in this hospital were studied with the purpose of demonstrating the frequency with which the blood is invaded by pneumococci and also of showing the rôle of pneumococci in the complication of this affection. The method used in making the blood cultures was essentially that which I described before this society last year in discussing the frequency of typhoid bacilli in the blood. In the later cases, however, instead of using bouillon, litmus milk was used as

a medium. The identity of the organism in each case was determined by its morphological, staining and cultural characteristics.

Pneumococci grew from the blood in 9 of the 30 cases tested, all of which ended fatally. The organisms were found in the blood only during short periods before death—from 3 days to 7 hours. In five fatal cases the organisms were not obtained, although in several of these cases cultures were made repeatedly.

From my results it may be concluded (1) that pneumococci invade the blood in only about 30 per cent of the cases; (2) that this invasion occurs mainly in fatal cases. While these cases all ended fatally, yet cases which recovered after cultivation of pneumococci from the circulating blood have been reported by Kohn, Sittmann, Petruschky and others. While my results in regard to the frequency of invasion of the blood agree with those of most other observers, yet within the past year several observers, especially Prochaska, have reported finding pneumococci constantly in the blood of pneumonia patients. His methods do not differ essentially from those we have used, and it is difficult to understand why our results do not agree. According to our results the procedure is of greater prognostic than of diagnostic value. An interesting question is what relation does the invasion of the blood bear to the fatal outcome. Does the patient die because the bacteria invade the blood, or do they invade the blood because he is dying? The results of the blood cultures probably explain why "in comparison with typhoid fever, pneumonia has but few complications and still fewer sequelæ," and also give the reason for the serious nature of the complications which do occur, namely, that they are usually but manifestations of a general pneumococcus infection.

In one of the cases of general pneumococcus septicemia in this series, arthritis and meningitis were present, without the occurrence of any acute lobar pneumonia, however.

Arthritis is one of the rare complications of pneumonia, and pneumococcus arthritis occurring independently of acute lobar pneumonia is still more rare. Another case of arthritis, from the joint of which pneumococci were obtained by Dr. Ladd, was treated in this hospital two years ago. The following are brief abstracts of these two cases.

CASE I.—Male, colored, aged 50. Admitted April 9, 1900, in a semicomatose condition. The patient had been sick for ten days with fever, delirium and cough. On examination some signs of involvement of the apex of the right lung were discovered, but they were not definitely those of consolidation. Two days after admission the left ankle appeared red and swollen, and was painful on motion and pressure. On the tenth day after admission the ankle joint was punctured and a syringe of yellowish, purulent, blood-tinged fluid removed. This fluid contained numerous pus-cells and red blood-corpuscles and many diplococci. Cultures made from this purulent fluid showed that these organisms were pneumococci. Arthrotomy was performed and the patient's condition at once began to improve, the temperature not becoming normal, however, until May 15—36 days after admis-

sion. The patient was discharged June 12. The ankle was still swollen but the incision had healed.

Whether this patient had a lobar pneumonia it was impossible to say definitely. Unfortunately no blood cultures were taken. During the illness a systolic murmur developed at the apex, decreasing much in intensity, however, before the patient was discharged. From the history and signs the probability is that a lobar pneumonia occurred primarily and that the arthritis and endocarditis (?) were secondary manifestations of a general infection.

CASE II.—Male, colored, aged 55, married. He was admitted February 13, 1901, complaining of pain in his joints. He was dull, and answered questions in a very vague, rambling, inaccurate manner.

For several years previous to admission he had had occasional attacks of pain and swelling in the joints. Both knee-joints had been swollen for four or five weeks before admission. Three days before admission he had had a slight chill. On the day previous to admission he appeared worse and during the night was delirious. He had had no symptoms pointing to pneumonia. On admission both knees and ankles were found to be red, hot and swollen, and there were indications of fluid in all these joints. There were no signs of pneumonia to be made out. There was marked stiffness of the neck and the patient's mental condition was apathetic.

On the morning following admission lumbar puncture was performed, the right knee-joint was aspirated and cultures were made from the blood. From the spinal canal about 20 cc. of turbid, pale-yellow fluid were withdrawn. The sediment was found to be composed of leucocytes and red blood-corpuscles. Both within and outside the leucocytes were seen many diplococci. These cocci in morphology and staining reactions resembled pneumococci and cultures made from this fluid showed later a pure growth of this organism. A purulent fluid was also obtained by aspiration of the knee-joint and in this also *Diplococcus pneumoniae* was demonstrated on cover-slips and later by cultures. The blood cultures also showed a pure growth of the same organism.

The patient gradually grew worse and died on the following day. The clinical diagnosis was pneumococcus septicaemia, meningitis and arthritis.

The autopsy showed a few minute areas of very fresh bronchopneumonia in the right lung, but there was nowhere any lobar pneumonia. An acute purulent leptomeningitis was present. The joints showed in addition to the acute purulent inflammation, the characteristic appearances seen in the joints in arthritis deformans.

It seems evident that in this case the joints were primarily infected owing to the old arthritis deformans rendering them loci minores resistentiae. No portal of entry for the infectious agent could be discovered. While the invasion may have been through the lungs, the clinical history and pathological findings point quite conclusively to the bronchopneumonia being secondary to the arthritis and general infection and occurring only as a terminal event.

In an article published last year in the *Lancet*, Cave col-

lected and reported 31 cases of pneumococcus arthritis. Since then I have found 11 others, including the two reported to-night. From a study of these cases it is found that there are two great groups:

I. Cases appearing as sequels or complications of acute lobar pneumonia.

II. Cases preceding or occurring independently of acute lobar pneumonia.

In this second group Case II certainly belongs, and possibly Case I. Including Case II, I have found the reports of eight such cases. In all these cases, except one which followed a puerperal peritonitis, the infection was primarily in the joints. In three cases the condition from the first was that of a pyemia with multiple foci. In all of the cases but one several foci appeared in succession. The occurrence of multiple lesions shows that in these cases there was probably an invasion of the blood by pneumococci, though Case II reported to-night is the only one in which this was demonstrated.

The three cases which were typically septicopyemias were all fatal. Of the other five cases, three recovered. In two of the cases there was a history of old chronic arthritis, and in one the infection occurred in a joint already the seat of a gouty deposit.

The following are some of the most important conclusions to be drawn from the study of all these cases of pneumococcus arthritis: The larger joints are the ones usually involved, though smaller joints may be involved. Usually more than one joint is involved in a given case (13 out of 41 cases). Joints already the seat of a chronic affection are most likely to be attacked. The effusion is usually purulent, but may be serous. The mortality is high, as out of 41 cases, 28 died. The clinical features and prognosis depend more on the septicopyemia, of which it is usually but a manifestation, than on the joint lesion itself. When recovery occurs the course is usually a long, slow one and usually ankylosis of the joint occurs. The local treatment should consist in free opening and drainage.

In one of the other cases of this series in which pneumococci were demonstrated in the blood there was also a meningitis. This is probably the most serious complication of pneumonia and is almost invariably fatal. It is also a rare complication and that two cases should have occurred in this series is quite remarkable.

In this second case, a typical one of acute lobar pneumonia in an alcoholic man, aged 38, peculiar respiratory symptoms appeared on the sixth day. The respirations became irregular and shallow and finally stopped, the patient becoming markedly cyanotic. As the pulse continued fairly good, artificial respiration was employed, but it was several minutes before spontaneous breathing occurred. Following this the respiration continued to show definite periods of apnea, lasting from 6 to 10 seconds, these periods separating groups of from 4 to 15 respirations. The pupils became unequal, there was external strabismus, and Kernig's sign was well marked. Definite convulsive movements occurred at inter-

vals, the extremities and back becoming rigid, the head being retracted and clonic movements occurring in the arms. Lumbar puncture was performed and 25 cc. of turbid fluid were obtained. Blood cultures were made at the same time. Following the lumbar puncture the convulsions continued for 5 or 6 hours, then stopped and the rigidity disappeared. The patient gradually became weaker, however, and died after several hours.

Pneumococci were demonstrated both on cover-slips and in cultures in the purulent fluid obtained by lumbar puncture, and they also grew in the cultures made from the blood.

A study of the clinical features in these two cases shows that in both the symptoms of meningitis were well marked, muscular rigidity and Kernig's sign being present in both.

Besides these two cases in which a meningitis was present, lumbar puncture was performed on three other cases in which the presence of a meningitis was suspected, but in each case the fluid obtained was perfectly limpid and cultures were negative. A review of the histories in these cases shows that in each case the symptoms were only mental, consisting of delirium, or in one case a state of coma vigil, while in none was there muscular rigidity or convulsions or presence of Kernig's sign.

#### DISCUSSION.

DR. FUTCHER.—In regard to the frequency of meningitis in connection with pneumonia, it might be of interest to refer to the statistics of 949 cases reported recently from the Boston City Hospital by Sears and Larrabee. There were 341 deaths, a mortality of 35.9 per cent. Clinically they diagnosed meningitis in 7 cases, but only three of these came to autopsy. They regarded these three cases as an expression of a general septicemia because each was associated with an acute endocarditis of pneumococcal origin. Autopsies were obtained in only 72 of the 341 fatal cases. In their cases no blood cultures were taken before death, but they took cultures in 62 cases post-mortem and found a general pneumococcus septicemia in 32 of these. So far as I remember there is no reference made to an arthritis in any of their 949 cases.

**The Distribution of Anopheles in the Vicinity of Baltimore.**  
MESSRS. HIRSHBERG and DOHME.

(See February-March BULLETIN, 1902, page 45.)

*January 6, 1902.*

The meeting was called to order by the president, Dr. Osler.

#### Coma in Cancer of the Stomach. DR. OSLER.

In the later stages of cancer of the stomach it is not uncommon to have mental symptoms, chiefly in the form of a slight delirium from the weakness and inanition, but there is in addition a remarkable coma resembling in some respects the well-known coma of diabetes. It is by no means common. There was no instance in the first 150 cases of cancer of the

stomach admitted to this hospital, the histories of which have been carefully analyzed in a monograph published last year by Dr. McCrae and myself. When, as in the instance here reported, coma comes on early in the disease, or when the symptoms of cancer of the stomach are not at all marked, it may be very confusing. An abstract of the case is as follows:

A. T. B., aged 58 (Gen. No. 37,311), admitted December 19, 1901, complaining of vomiting and progressive weakness. He had been a healthy, active man, of fairly good habits; had served four years in the army. He had been a dyspeptic all his life. He had frequently had nausea, but had never vomited until his present illness.

Early in September of 1901 he had an aggravation of his dyspepsia, with a great deal of pain and burning in the stomach. The pain, the only unaccustomed feature, was of a gnawing, burning character, and was increased by taking food. He had lost in weight and had loss of appetite. Vomiting had occurred recently. He continued at work until three weeks ago. The weakness has been progressive, and he has had to go to bed. He has been cold and nervous and very apprehensive. The vomiting during the past week has been very severe, so much so that his doctor used rectal feeding. He has never vomited blood or large amounts. The loss in weight has been rapid, twenty-five pounds in the three months.

On admission the patient looked ill and emaciated, with a very dry skin. Examination of the thorax showed nothing of any moment, except feeble, distant heart sounds. He had an unusual degree of sclerosis of his radials with calcification.

In the note made on December 19, Dr. McCrae noticed in the left half of the epigastrium "a nodular thickening feeling like the pylorus." The liver was not enlarged. The examination of the vomitus showed a total acidity 30, free hydrochloric acid 10, no lactic acid. Microscopically no formed elements, only a few leucocytes and some yeast cells.

Both Dr. McCrae and I repeatedly examined the abdomen, and we discussed together the character of a rounded transverse body noted in the epigastrium, but we never arrived at a definite conclusion as to its nature.

He was a very nervous and apprehensive man, and had had worries, and this, with the negative condition of the vomitus, made us hesitate in the diagnosis of malignant disease, though Dr. McCrae had suspected it at first.

On December 28, after a few days of improvement, he appeared very dull and drowsy and slept almost the entire day. When aroused he was irrational. During the 29th he was semi-comatose all day, replied to questions in a confused manner, then sank into a state of lethargy, with his eyes open, but not recognizing his surroundings. The respirations were shallow and frequently of Cheyne-Stokes character. There was no Kernig's sign, no retraction of the head.

On the 31st he was so very comatose that we suspected the possibility of a terminal meningitis in a case of old arteriosclerosis, and I asked Dr. Theobald to see him. He deter-

mined the presence of a commencing optic neuritis with swelling of the discs and edema of the surrounding retinae. Lumbar puncture was performed, and 30 cc. of clear fluid removed, which came off with considerable tension. On the evening of the 31st his temperature began to rise, and rose to nearly 103° throughout the 1st, and he died at 6.15 P. M.

The urine was, as a rule, of normal specific gravity, 1018 to 1022. He passed about 1500 cc. There was the faintest trace of albumin, no sugar, and there were many hyaline and finely granular casts. The urea was .028. There was a marked reaction for acetone and diacetic acid.

The autopsy, made by Dr. MacCallum, showed a small carcinoma in the pyloric zone, beginning to ulcerate, not invading the pyloric ring. From its situation evidently this was the small tumor which Dr. McCrae had felt at the first examination. The heart was small, rather atrophic, the coronary arteries exceedingly sclerotic, and a diffuse general arteriosclerosis. The kidneys were a little under-sized, red, markedly granular and cirrhotic. There was no meningitis. The convolutions were much atrophied, and there was an unusual quantity of cerebrospinal fluid.

The cause of the coma is unknown—whether a special poison produced by the cancer (which is unlikely) or an acid intoxication similar to that which occurs in diabetes, which is suggested by the presence of acetone and diacetic acid in the urine, or whether it was uremic, which is favored by the state of the kidneys. In any case the clinical features presented by this patient were of unusual interest.

#### A New Study of Snake Venom. DR. SIMON FLEXNER.

Dr. Flexner presented the results of a study of several kinds of snake venom upon mammalian blood and tissues and upon bacterial life. He stated that the study was conducted by Dr. Noguchi and himself at the suggestion of Dr. Mitchell, with whom many of the experiments were arranged.

This study, which is here in an incomplete form, has proven the agreement between the venoms and other body fluids, such as blood serum, and toxins of vegetable origin, such as bacterial toxins, ricin, etc.

Among the first experiments made were those relating to hemolysis which showed that the solution of blood-corpuscles in animals was produced through the interaction of intermediary bodies and complements. The intermediary bodies were supplied by venoms; complements, by serum in which corpuscles were suspended. When corpuscles free from serum were brought into relation with venoms in suitable quantity, no solution occurred but only agglutination of the corpuscles. The agglutination is produced through the action of principles different from hemolytic agents, as could be proven by the removal of the agglutinated corpuscles when the clear fluid is still able to cause hemolysis under suitable conditions.

The agglutinating power of venoms is destroyed by temperatures of 75°-80° C., maintained for 30 minutes. Temperatures of 75°-80° C. maintained for 30 minutes have no effect upon the hemolytic action of any kind of venom.

At temperatures of from 90°-96° C., crotalus venom in solution suffers a moderate reduction in hemolytic power, while that of the copperhead, cobra, and water-moccasin are unaffected. After heating to 100° C. for 15 minutes the dissolving power of these upon red corpuscles is slightly reduced. There is no dissolving action upon corpuscles at freezing temperatures. If, therefore, corpuscles which have been treated with serum for thirty minutes at zero temperature are separated by centrifugalization, the complement of serum is unaffected while the intermediary body is found to have been removed from the serum by the corpuscles. In this way the complement for a particular species of corpuscles free from intermediary body can be obtained. The addition of such complement-containing serum to venomized washed corpuscles of a similar species brings about hemolysis. While the addition of fresh washed corpuscles to this treated serum, from which the intermediary body for them has been removed, is unattended by solution. The action of complements freed from any intermediary body upon venomized corpuscles of different species by this means has also been studied. The results have led to the following conclusions: (1) Venom contains several or many intermediate bodies; (2) These bodies show specific affinities for certain complements. In addition to this there is evidence that the many susceptible corpuscles contain, besides specific haptophore groups for intermediary bodies, certain common haptophore groups which are shared, perhaps, by all vulnerable corpuscles.

The effect upon white cells freed from red cells was also studied. Accumulations of leucocytes were induced by introducing dead cultures of *B. megatherium* into the pleural cavity. The observations were made on a warm stage. The first effect is agglutination, after which disintegration of cells takes place. After six hours the majority of the largest granular cells have already disintegrated, the nuclei having been liberated. After twenty-four hours most of the medium-sized granular cells have suffered disintegration, while the lymphocytes show but slight and inconspicuous changes. Stronger solutions of venom varying from 0.2 per cent to 10 per cent cause instant cessation of motility and rapid agglutination without distinction of variety of cells. Within five to thirty minutes thereafter dissolution sets in, affecting, first, the largest, then medium-sized cells, and finally the small lymphocytes.

The effects upon washed leucocytes differ from those described, in that venom solutions cause agglutination, but with the production of only very slight lysis. It could also be shown that while the agglutinating principles may be identical both for white and red cells, the dissolving principle for leucocytes is distinct from that for red cells.

Venom toxicity with especial reference to the determination of the existence of neutralizing substances for venom in the tissues of the body was studied. Brain, liver, spleen, kidney, voluntary muscle, adrenal gland, and blood were brought into intimate contact with venom. After centrifugalization, the clear fluid was injected into guinea-pigs. It

was found that the brain alone, when used in sufficient quantities, was capable of detoxicating venom.

In comparing the neurotoxic and hemolytic principles it could be shown that they are physiologically distinct. Moreover, that while the chief toxic constituent unites with the nerve cells, in venom from which the neurotoxic principle has been removed a quantity of hemolysin may be contained sufficient to bring about fatal intoxication.

These results are in keeping with the views expressed by Ehrlich, and supported by Wassermann, and Takaki's experiments on the fixative power of cells for certain groups of toxic substances.

The effects of venom upon the bactericidal properties of blood serum were also studied. The bactericidal effects of normal sera having first been established for *B. typhi*, *B. coli*, and *B. anthracis*, the influence of venom was next studied. It was found that the bactericidal property was destroyed by venom, as had previously been shown by Welch and Ewing, the mechanism of this destruction consisting in the fixation of serum complements by venoms; and that no action is exerted upon the intermediary bodies of the serum.

Antivenin neutralizes the venom both in regard to hemolytic and antibactericidal actions.

#### **Digestive Processes in Carcinoma of the Stomach. DR. EMERSON.**

(See April BULLETIN, 1902, page 91.)

*January 20, 1902.*

The meeting was called to order by the president, Dr. Osler.

#### **Exhibition of Surgical Cases. DR. HALSTED.**

Dr. Halsted exhibited a case of gall-stone in the common duct, the patient having suffered for about four years, with a pretty definite history of obstruction. A stone was found in the common duct as large as an egg. The patient had no trouble after the operation, and made a rapid recovery.

The second case was that of an abscess of the liver, admitted to the hospital on November 10, 1901, after an illness of ten weeks. Here a small quantity of reddish brown pus was removed by operation, and the patient made a good recovery. An interesting feature of the case was the great cyanosis which was present.

#### **DISCUSSION.**

DR. CULLEN.—In June I saw a case where the patient had been expectorating considerable pus for three or four years. She had some temperature and a great deal of pain over the region of the liver. Her physician thought at the time that it might be gall-stones, but there was no evidence of jaundice. At the operation I found the gall bladder perfectly normal but there were adhesions between the surface of the liver and the anterior abdominal wall. On gently

separating them we obtained about three drams of pus from the upper surface of the liver. The cavity was packed off and drained, and as the temperature dropped to normal the patient was allowed to return home, but she still expectorates purulent matter. I would like to ask Dr. Halstead if he has had such a case and if he thinks it was due to a perforation into the lung.

DR. HALSTED.—Was there any chance of peritonitis?

DR. CULLEN.—No. It evidently came from the pleural cavity.

DR. OSLER.—In reference to this last case, there are two or three points of interest. In the first place, the position of the swelling over the sixth or seventh ribs and along the right costal border suggests to the non-surgical eye enlargement of the ribs themselves. Rather against the view that we had an abscess of the liver, particularly at first, was the fact that there was no fever, no leucocytosis, and there was a singular absence of tenderness on deep pressure. As a rule, when there is an abscess of the liver if you press hard enough there is some wincing.

The first case shown by Dr. Halsted illustrates the importance of a diagnosis. That unfortunate woman, the wife of a physician, too, had gone all over the country seeking a diagnosis but getting only treatment. Any one at all familiar with recent work on the liver could have made it easily; in fact my secretary, to whom a young physician dictated the notes of the case in my absence, made the diagnosis from his description.

#### **Exhibition of a Case of Syringomyelia. DR. THOMAS.**

(To be published later.)

*February 3, 1902.*

The meeting was called to order by Dr. Hurd.

#### **Peripheral Venous Thrombosis in Pneumonia. DR. WALTER R. STEINER.**

(See June BULLETIN, 1902, page 130.)

#### **Exhibition of a Case of Thrombosis. DR. WARFIELD.**

This patient, a colored man, twenty-seven years of age, was admitted January 4, 1902, complaining of fever and pain in the side. His family history was negative and the only thing of interest in his personal history was two previous attacks of pneumonia, both of which were very severe. He came in with a gonorrheal urethritis. His present illness began on December 25, and on the 31st he developed a pain in the chest with fever, cough and expectoration. When he entered the hospital he was markedly cyanosed, his respirations were shallow, 80 to the minute, and his pulse was both intermittent and irregular. He was in such bad shape that it was necessary to stimulate him immediately and he was put on digitalin and strychnia. He was also ordered ice sponges every three hours. His pneumonia was found to be on the left side, taking up the entire left lung. The next

morning the patient was decidedly worse, the heart sounds, which the night before were barely audible, were then inaudible except at the apex, where they could be faintly heard. He was then infused with 500 cc. salt solution, and as his condition improved, he was given another injection of 1100 cc. later in the day. For 48 hours he was in a critical condition and then his temperature began slowly to come down. His lungs showed no change on the left side, but on the right side it was noticed that in the axilla and on the back there was impaired resonance. His leucocytes dropped from 21,000 on admission to 8000, then went up to 17,000, and towards the end of his illness dropped again to 2500. He gradually improved, never at any time being delirious.

On the 21st day of his disease, his temperature was normal and he did well from that time on until January 26, when the left lung was practically clear. The patient had been up in a wheel chair for several days when he complained of pain in the right leg beneath the knee, and on examination it was found that there was acute tenderness in the popliteal space and a cord-like swelling could be felt extending down the leg, which could be followed in two or three branches of the vessel. This swelling was very tender, but there was no tenderness along the femoral vein. The leg was immediately wrapped in cotton with a lead and opium lotion, and the patient kept perfectly quiet in bed. He improved markedly until the 31st when he developed an acute epididymitis which sent his temperature up to 102.4°, but his general condition rapidly improved and there was never at any time any swelling or edema of the leg. His recovery from that time on has been steady.

#### Inorganic Ferments. DR. JONES.

(See May BULLETIN, 1902, page 97.)

February 17, 1902.

#### Exhibition of Cases. DR. CULLEN.

**CASE I. HYDATIDIFORM MOLE.** The patient was referred to me by Dr. Johnston, of Berkley Springs, W. Va., on April 8, 1901, complaining of a uterine enlargement associated with backache. Five months previous to our examination she had missed her period for two months and since then there had been a continuous very dark red vaginal discharge. The uterus was uniformly enlarged and the size of a three or four months' pregnancy, while the cervix was very hard and the os small. Myoma was first suspected but we decided to explore the uterine cavity as the temporary cessation of menstruation followed by the very dark discharge was strongly suggestive of a dead fetus. On dilating the cervix and introducing the curette fully half a litre of cyst-like bodies was removed. These varied from a pin to a cm. or more in diameter. The patient made a prompt recovery.

Gynecological pathological No. 4851. The specimen consists of about half a litre of small transparent cysts varying from one to two cm. in diameter. These are thin-walled and immediately remind one of small subperitoneal cysts. They

are traversed by a delicate net-work of blood-vessels. The exact relation of the majority of the cysts cannot be determined as they were brought away with the curette. Here and there, however, we have been fortunate enough to obtain large pieces of the growth. At such points we find shreds of membrane and attached to these by delicate pedicles varying from 1 mm. to 2 cm. in length are these delicate and small cysts (Fig. 1). On examining these cysts further some of them are found to be pear-shaped instead of round. Accompanying the cysts are large and small shreds of solid tissue, no doubt portions of the decidua.



FIG. 1.

A SMALL FRAGMENT OF A HYDATIDIFORM MOLE (Natural size).

Gynecological pathological number 4851. The specimen has been floated out in water in order that the ramifications may be followed. *a* corresponds to the basal attachment and *b* is a large cystic dilatation of a villus. At *c* we have rows of small oblong cysts. The main stem continues downward and spreads out into the conglomerate mass of cysts *d*, but just above this point it gives off a small stem of stroma which ends in a cystic terminal *e* after having given off two terminal twigs *f* with cystic ends. At *f* is a cystic dilatation in the continuity of a villus; a short distance further on followed by the terminal bunch of cysts *g*.

**Histological examination.**—Sections from the cysts show that the outer surfaces in places have a covering of syncytium very scant in amount. At most points, however, this is wanting. The walls consist of spindle-shaped cells and the

inner surface has clinging to it coagulated fluid. There is no layer of cells lining the inner surface of the cysts. These small tumors are due to cystic dilatation of the stroma of the villi and hence are not true cysts. In some places typical villi are demonstrable. Covering the outer surface of some of the villi and lying in close proximity to the cysts are masses of cells somewhat resembling decidual cells. They are, however, much larger than ordinary decidual cells. The nuclei are also larger, are irregular and stain deeply. All gradations from those of normal size to the large and irregular ones can be followed. While the majority of these cells are probably decidual in origin, some of them are undoubtedly altered syncytial cells, as the direct transition can be traced. Given such cell changes apart from pregnancy, we should not hesitate to pronounce the growth malignant, but occurring with the hydatidiform mole we cannot give a positive diagnosis.

In a case like this it is wise to watch the patient carefully and if any suspicious signs, such as bleeding, develop the uterus should at once be curetted and the tissue examined histologically. In this case, as seen from the clinical report, the patient had no further trouble. On account of the suspicious histological findings we kept the woman under close observation for several months but she failed to show the slightest symptom suggestive of deciduoma malignum. I examined her on October 5, 1901, and found the pelvic organs normal. At the present time she is perfectly well. In all cases of hydatidiform mole we should make a very careful histological examination to determine if there be commencing deciduoma malignum. Neumann, who has been especially interested in this subject, examined eight moles and found that three showed distinct malignant changes. These three subsequently developed deciduoma malignum.

**TUBERCULOSIS OF THE KIDNEY.**—This patient was referred to me by Dr. J. B. Merritt, of Easton, complaining of loss of weight and of slight frequency in micturition. She is fairly well nourished, 47 years of age. On cystoscopic examination we found slight reddening around the left ureteral orifice. The right showed no change. On catheterization the urine from the right kidney gave some albumin, the left yielded myriads of tubercle bacilli, a single field containing hundreds of them. At a second examination of the left kidney it yielded a similar result. The principal part of the tuberculous process proved to be at the upper pole of the pelvis and the eye of the catheter had burrowed into tuberculous tissue. We were loath to remove the entire kidney, but on account of the wide dissemination of the tuberculous process it was impossible to save any portion of it. Prior to operation Mr. Broedel suggested excising a portion of the 12th rib in order that we might have plenty of room. The chief difficulty in performing nephrectomies is that considerable tension has to be exerted on the kidney during its enucleation and the operator is afraid of tearing the renal vessels or of rupturing an accessory artery. By resecting a portion of the rib the space is augmented by half or more and one is enabled to control the vessels under sight

and with the utmost ease, and this operation that may sometimes be difficult is thus rendered an easy one and the kidney is delivered without any tension of its vessels.

The incision was commenced from the lower margin of the 11th rib, continued downward and slightly forward until about two inches above the crest of the ileum and was then continued forward parallel with the same. The skin flap was dissected forward until the margin of the latissimus dorsi was exposed (Fig. 2). The 12th rib was then located and the latissimus severed until the requisite amount of rib was exposed. The periosteum of the rib is peeled back and from two to three inches of the bone removed. The superior lumbar trigonum is now fully exposed and the kidney lies directly beneath the opening thus obtained (Fig. 3).

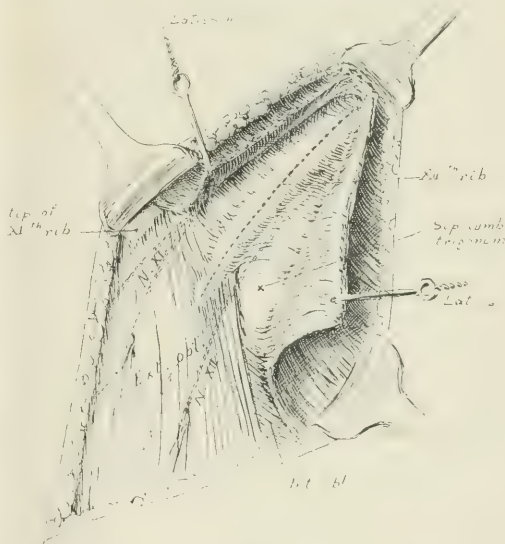


FIG. 2

#### EXPOSURE OF THE 12TH RIB PREPARATORY TO PARTIAL RESECTION.

The edge of the latissimus dorsi has been located and then the muscle has been severed directly over the rib and drawn to either side. The rib and the superior lumbar trigonum are thus exposed. The periosteum of the rib is incised as indicated by the dotted line, the bone shelled out and removed.

This operation with slight modification has been employed by several German surgeons with good success. There is a possibility of opening the pleural cavity if care be not exercised, but should such an accident happen the cavity can be closed by suture at once. Dr. Halsted has employed this method once, and since our operation Dr. Hunner has also removed a portion of the rib prior to performing nephrectomy. I feel confident that in the future the advantages offered by this method will find a wide use. Our patient made an uneventful recovery.

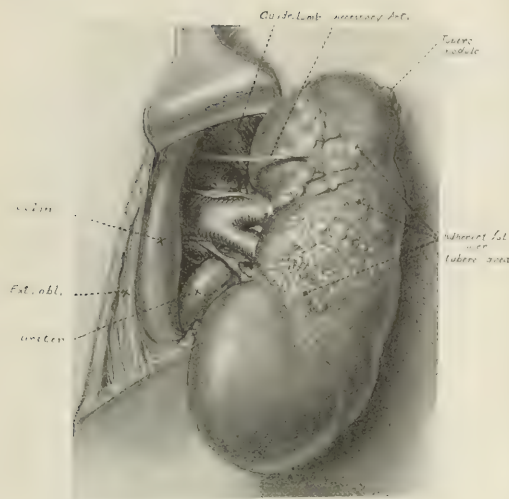


FIG. 3.

## RENAL EXPOSURE OBTAINED BY PARTIAL REMOVAL OF THE 12TH RIB.

The incision is directly over the kidney, allowing the organ to be delivered without any downward traction and with practically no tension on the vessels. Any accessory vessel is at once recognized and tied and all renal vessels are well exposed for ligature.

## DISCUSSION.

DR. HUNNER.—The case Dr. Cullen referred to is a patient in the ward at present, operated on nine days ago by the method he describes. It was a case of tuberculosis of the kidney, ureter and bladder. The kidney was three or four times larger than normal, and its removal through the usual incision would have been extremely difficult; but with the removal of the twelfth rib, the operation was comparatively easy.

After excision of the kidney I removed the ureter and a portion of the bladder through an extraperitoneal inguinal incision. This was done without tying or cutting the uterine vessels, a procedure which I have not before seen described. By strong traction on the ureter, and forward displacement of the uterine vessels by means of a blunt spatula, a cone-shaped area of the bladder wall was easily exposed. Before resecting the diseased area a row of interrupted catgut sutures was placed—each end penetrating the bladder wall just beyond the margin to be cut. This anticipated the difficulty of placing sutures after the removal of the ureterovesical region, and the consequent retraction of the bladder beneath the uterine vessels.

In addition to the tuberculous area immediately about the ureteral orifice, cystoscopy had revealed a large ragged ulcer, three to four centimetres in diameter, in the vertex of the bladder. The operation was finished by removing this ulcer through a suprapubic extraperitoneal incision. The bladder

was closed with catgut and a retention catheter was introduced through the urethra. Each of the three incisions was partially closed and a gauze drain was inserted to the bottom of each. The entire operation occupied two hours.

EXTRA-UTERINE PREGNANCY FOLLOWING OLD SALPIN-  
GITIS.—Every year the surgeon is growing more conservative in dealing with the tubes and ovaries, and many of these structures that were formerly removed are now preserved in part or in their entirety. When advocating carrying out this commendable conservatism occasional drawbacks must not be forgotten. Recently two striking cases have come under my care.

CASE I.—Seen in consultation with Dr. Frank R. Smith. The patient was 26 years old. We found old tubal adhesions on both sides. These were readily broken up on bimanual examination under ether and at the same time I dilated and curetted. For several weeks subsequent to the examination the patient received a regular bimanual massage with much benefit. I lost sight of her for two years, when again called in consultation by Dr. Smith. The patient had missed her period for about five weeks and then passed some clots which she took for a miscarriage. Previous to this she had done some heavy lifting and following the hemorrhage she had not taken the usual precautions but was up and around nursing a sick relative. When I saw her she had a temperature of 100°, excruciating pain slightly above the umbilicus and in the mid-line. She was very pale and felt that she would die unless something were promptly done. On vaginal examination a distinct bulging could be made out in the vault, but on account of extreme sensitiveness and abdominal rigidity nothing further could be determined. She was immediately removed to the hospital. On opening the abdomen we found a ruptured tubal pregnancy on the left side, the side on which the most adhesions were found two years previously. The pelvis was filled with dirty fluid and dark clots. The great pain experienced just above the umbilicus in the mid-line was due to almost complete obstruction of the bowel. Two small clots lying on the mesentery of the small intestine had become partly organized and were growing together. They were contracting in such a way as to almost completely constrict a knuckle of the small gut. At the point of constriction the outer surface of the intestine was already covered by a thick layer of fibrin and we would have had general peritonitis in a few hours. The patient, although pulseless when leaving the table, made a good recovery.

CASE II.—Seen in consultation with Dr. Rubinstein in April, 1899. The patient was 26 years of age, and on examination we found marked induration in the pelvis and there was considerable temperature. Douglas' sac was opened from below. On the right side we found a small tuboovarian abscess from which about 30 cc. of pus was removed. On the left side numerous adhesions were broken up. Drains were introduced and the patient made a good recovery. She had no further trouble until June of 1901.

Two years after the first operation she missed her period for two weeks and then had the characteristic bloody discharge. Her physician found some thickening and reddening of the cervix and asked her to return in a few days. In the meantime she suffered sudden collapse, and on examination gave distinct evidence of hemorrhage. I saw her several days after this. The pulse was almost nil, the patient was blanched and breathed with difficulty. On vaginal examination a firm mass bulged in the vagina. This filled the entire pelvis and was continuous with a distinct area of hardening filling the lower two-thirds of the abdomen. Although the patient was exceedingly weak we advised immediate operation. The abdomen was opened two hours later. About 3 litres of coagulated and dark blood were removed from the abdominal cavity. On the left side, the side where we had no pus and numerous adhesions at the previous operation, we found a ruptured tubal pregnancy and a two months' fetus. On the right side was an abscess fully 10 cm. in

diameter. We hardly expected this patient to recover, but in a few weeks she was up and around again. At present she is perfectly well.

These cases illustrate well the fact that old tubal adhesions or chronic salpingitis may be the cause of tubal pregnancy probably due either to the diminution in the vermicular action of the tube which normally assists the ovum to reach the uterus or to small recesses formed by tubal folds adhering to one another. These cases also illustrate, as was mentioned above, some of the disadvantages of conservative work. Taking everything into consideration, however, we have no hesitancy in advising the utmost conservatism, as the advantages far outweigh those of complete removal of the organs.

#### Demonstration of a New Combined Cantery Incision for Prostatic Hypertrophy. DR. YOUNG.

(See February-March BULLETIN, 1902, page 36.)

### NOTES ON NEW BOOKS.

A Text-Book of Pharmacology and Some Allied Sciences: Therapeutics, Materia Medica, Pharmacy, Prescription Writing, Toxicology, etc. By TORALD SOLLMANN, M.D., Assistant Professor of Pharmacology and Materia Medica in the Medical Department of Western Reserve University, Cleveland, Ohio. Illustrated. (Philadelphia and London: W. B. Saunders & Co., 1901. pp. 894.)

No American book upon this subject since the appearance of that of Dr. Cushny's has been so welcome as the one before us, for it indicates that the younger American writers at least intend to deal with the subject of therapeutics and materia medica from a scientific standpoint, thus bringing this department of medicine into the proper relation to other departments which have long ago been treated in a scientific spirit. The book before us contains much that is of value both to the student and the practitioner and numerous therapeutic suggestions not often found in similar books. It is divided into four parts: Part I being general in character and treating of such subjects as the gross anatomy of plants, the metric system, pharmaceutical methods, especially pharmaceutical preparations, prescription writing and the like. Part II treats of Pharmacology, Therapeutics and Materia Medica, and this embraces the major portion of the book, about 600 pages. The drugs, in similar manner to that adopted by Cushny, are divided into groups, such as the strychnine group, the cocaine group, the quinine group, etc., and the old nomenclature so long in vogue of separating the drugs into expectorants, depressants, hypnotics, etc., has been abandoned.

Part III is devoted to practical exercises as a laboratory guide and might be of some value to the student who was working independent of an instructor. In this part one chapter is devoted to animal experimentation.

Part IV, embracing an Appendix, treats of methods of analyzing the causes of pharmacologic action, and a table made up from Maisch's Organic Materia Medica, the crude organic drugs by orders and the inorganic or chemie with their formulas, solubility and dose.

If there is any criticism to be made of the book it is that there seems to be little logical method in the arrangement of

Part II. One subject follows another without that logical sequence which might justly have been expected, and further the pages are so divided up by the introduction of various sized types that the result is confusing, rather than helpful. Many notes, often containing most important suggestions, are introduced in very fine type, and the page is broken into so many paragraphs that it has a jerky effect upon the mind in reading. However, the book is written in the right spirit and must be exceedingly useful in directing students and practitioners into the proper line of thought in dealing with this important branch of our work.

Nursing, General, Medical and Surgical, with Appendix on Sick-Room Cookery. By WILFRED J. HADLEY, M.D., F.R.C.P., Physician and Pathologist to the London Hospital, etc. (Philadelphia: P. Blakiston's Son & Co., 1902.)

This book was written primarily for the use of English nurses in England and some of the directions which it gives are not well adapted to this country. Thus, for example, the statement that the sick room should be kept at a temperature of 60° F. and that it should rarely be allowed to fall to 50° would hardly be accepted in America. The same is true of some of the apparatus mentioned which bear names not in common use here. Taken as a whole, however, the book is a very handy little manual and can be freely recommended for the instruction of nurses. The volume is neatly printed and very attractive.

A System of Physiologic Therapeutics, a practical exposition of the methods other than drug-giving, useful in the prevention of disease and in the treatment of the sick. Edited by SOLOMON SOLIS COHEN, A.M., M.D., Professor of Medicine and Therapeutics, etc. Vol. VI, Dietotherapy and Food in Health. By NATHAN S. DAVIS, JR., Professor of the Principles and Practice of Medicine in Northwestern University Medical School, etc. (Philadelphia: P. Blakiston's Son & Co., 1901.)

The other volumes in this series have been reviewed at length in the BULLETIN. Volume VI is divided into two parts,

"General Principles of Diet and Diet in Health" and "Diet in Disease." The first part contains much information as to the value of various articles of food and the best dietaries for persons in health, such as athletes, brain-workers, infants, children and the like. Tea, coffee and alcoholic beverages all receive due attention but nothing new is presented in regard to them. In the second part the directions given as to dietaries in various diseases like typhoid fever, dysentery, infectious diseases and diseases of the stomach, lungs, circulatory organs, kidneys, nervous system, skin and intestines are clear and concise and must be most helpful to the physician who is called upon to treat these disorders. The volume contains an excellent index and its rich stores of applied knowledge are thus readily accessible. The book is one of the most valuable of the series.

**Diseases of Women:** A manual of Gynecology designed especially for the use of students and general practitioners. By F. H. DAVENPORT, M.D., Assistant Professor in Gynecology, Harvard Medical School. Fourth edition, revised and enlarged with 154 illustrations. (Philadelphia and New York: Lea Brothers & Co., 1902.)

The object of this little book is to give the student clearly but with considerable detail, the methods of examination and the simple forms of treatment of the most common diseases of the pelvic organs and also to help the busy practitioner to understand and treat the gynecological cases which he meets in his everyday practice.

The chapters on anatomy and diagnosis are clearly and concisely written and well calculated to help the student and the general practitioner. In the matter of treatment the book seems not wholly in accord with modern methods. The use of pessaries for displacements, of the uterine probe, of local applications of glycerite of tannin, etc., are doubtless survivals of the first three editions and probably would not occupy as much space in the present edition if the work had been wholly rewritten. With these minor exceptions the work is worthy of much praise.

**Syphilis.** A Symposium. Special contributions by L. DUNCAN BULKLEY, F. CABOT, JR., L. A. DUHRING, PROF. FOURNIER, E. FULLER, E. B. GLEASON, M. S. GOTTHEIL, R. H. GREENE, N. B. GWYN, O. HORWITZ, E. L. KEYES, G. F. LYDSTON, D. J. MCCARTHY, T. G. MORTON, B. REED, A. ROBIN and J. D. THOMAS. (New York: E. B. West & Co., 1902.)

This book is composed of articles which were originally published in the International Medical Magazine, and are here republished because of a demand for the articles in an accessible form. The most valuable portion of the book is to be found in the answers to half a dozen questions in reference to the diagnosis and management of syphilis. The book contains much useful information upon this important subject in a readily accessible form.

**Manual of Childbed Nursing with Notes on Infant Feeding.** By CHARLES JEWETT, A.M., M.D., Sc.D., Professor of Obstetrics and Diseases of Women in the Long Island College Hospital. Fifth edition, revised and enlarged. (New York: E. B. West & Co., 1902.)

This is a practical book prepared by a teacher for the use of nurses. It contains concise and specific directions for the guidance of an obstetrical nurse in the care of her patient during the puerperium. Directions are given for the preparation of the patient and her bed, for the care of the patient during labor, including the sterilization of all articles which require to be used before labor and the dressings to be employed

thereafter. The chapter on the prevention of childbed infection is a valuable one. There are also chapters on the "Care of the Child," on "Artificial feeding" and on "Management of the Birth in the absence of the Physician." If any criticism is to be offered it must be that the book is possibly too concise and brief. A greater latitude on the part of the author in using his materials would undoubtedly have added to its interest and value.

**The Roentgen Rays in Medicine and Surgery as an aid in Diagnosis and as a Therapeutic Agent, designed for the use of Practitioners and Students.** By FRANCIS H. WILLIAMS, M.D. (Harv.) With 391 illustrations. Price \$6. (New York: The MacMillan Co. London: MacMillan & Co., Ltd., 1901.)

The first chapter states clearly and concisely some of the known important properties of the X-ray and especially those which relate to medicine and surgery. In this chapter is given an illustration of 20 radiographs of equal bulks of various substances found in the human body. The writer states: "This experiment suggests how we may recognize some changes in chemical composition made in the body by pathological processes. The ability to do this without beaker or reagent or without disturbing the vital processes is a step in the application of chemistry and physics to practical medicine which hints at what the future may have in store for us."

In considering the subject of an X-ray equipment the static machine and induction coil are both considered and the writer very carefully describes the mechanism of both machines and especially the management of the forms with which he has worked. Tubes, tube-holders, the fluoroscope, the methods of examining the patient and recording the findings receive the same detailed and careful description.

The appearances seen in pulmonary tuberculosis are described, also the actual conditions in the lung and the restricted movements of the diaphragm on the affected side.

The writer subdivides the classes of cases of pulmonary tuberculosis in which the X-ray examinations are of value as follows: In cases where there are no physical signs or where they are very doubtful; where there are slight physical signs only; where an accompanying emphysema, bronchitis, pleurisy or pneumonia may disguise the physical signs of tuberculosis; where the physical signs indicate a tuberculosis which the X-rays do not confirm; where tuberculosis of other organs being present it is desirable to ascertain if the lungs are affected; where a tubercular family history may require precautionary X-ray examinations.

An X-ray examination is also of value in old tuberculosis; in determining the progress and extent of existing disease; in determining whether a patient should or should not remain at home; in acute miliary tuberculosis and in lung cavities.

In conclusion he points out what the early diagnosis of incipient tuberculosis means and the importance of any and all aids. Aside from the information obtained from inspection, percussion and auscultation we now have a third method, namely, the X-ray examination. "We may by these not only control one method by another but with the eye supporting the ear we also control one sense by another."

Other pulmonary conditions are considered, as emphysema, pneumonia, pleurisy, empyema, hydrothorax and pneumothorax, etc. Its value in the diagnosis of central pneumonia is emphasized.

Its aid in forming a differential diagnosis is pointed out and also the importance of looking for the primary cause of the trouble in some other organ. As for example, the darkening of the bases of the lungs may not primarily be due to pulmonary but to renal or cardiac disease. The heart and thoracic

conditions, other than pulmonary, as aneurisms, new-growths, receive the same attention.

The chapter on the therapeutic uses of the X-rays gives the experiences of the writer and others up to the time of the publication of the book. Cases are reported showing its beneficial effect on lupus and superficial epithelioma. The possibility of a return of the new growth is considered and the writer passes over the treatment of more deeply-seated growths on account of insufficient data. Methods of applying the X-rays to therapeutic uses are given and the dangers of dermatitis are considered.

The results of various investigators as to the effect of the X-rays on bacteria are given. It seems that the growth of the bacteria outside of the body may be hindered by means of the X-rays.

The following uses of the X-rays in surgery are treated of: In fractures and dislocations of bones, in the detection of foreign bodies, in diseases of the bones and joints, in congenital malformations, in dentistry and in the detection of calculi.

Its importance not only in making a diagnosis is set forth but also in seeing the results and progress of treatment.

The medical profession is much indebted to Dr. Williams for publishing this work. Its special value lies in the fact that so much of it consists of his own experience and that cases are given, not only with X-ray findings illustrated by tracings, diagrams and radiographs, but also with the description of the physical signs so that one may be compared with the other. The writer states in one part of the work that "X-rays are a most effective method of showing how great a rôle the imagination may play when using auscultation and percussion." Without trying to belittle the writer's work and granting the great aid the use of X-rays are in surgery and medicine, most of us must confess that the interpretation of the X-ray findings offers a large field for the play of the imagination, which diminishes in size as the experience of the physician in this branch of work increases.

The surgeon may complain that internal medicine receives twice as many pages as surgery. But we must remember that the application of the use of the X-rays to internal medicine is a newer field and one that the writer is especially interested in. For that reason the work is all the more valuable.

*A Laboratory Guide in Elementary Bacteriology.* By WILLIAM DODGE FROST, M. S., Instructor in Bacteriology, University of Wisconsin. Illustrated octavo, second revised edition. (Published by the author, Madison, Wis., 1902.)

This admirable book is not an addition to the already rather large number of text-books on bacteriology, but is, as the name indicates, a guide in laboratory work, designed to be used in connection with any of the standard texts, to which there are numerous references. Part I, entitled General Bacteriology, contains the usual classical exercises by means of which the student learns bacteriological methods, a systematic study of non-pathogenic bacteria, and a few pages devoted to the bacteriological analysis of air, water, and milk. The treatment of the Physiology of Bacteria is more complete than that usually found in books of this kind, and the exercises easy and practical. Part II, entitled Medical Bacteriology, includes the study of pathogenic bacteria, animal inoculation and staining of bacteria in tissue, bacteriological diagnosis, and the detection of pathogenic bacteria in water and milk supplies. Part I also contains a chapter on taxonomy. Migula's classification is used and the binomial nomenclature approved by scientific bacteriologists is preferred, the more commonly used names being given as synonyms. For the purpose of study, however, the bacteria are gathered in convenient groups. Blank charts of the various organisms offer the

student a means of recording his observations, and blank pages are for the purpose of preserving notes and references.

The exercises presented have been thoroughly tried and approved by the experience of the author. They are arranged in a manner which will allow them to be adapted to the use of any teacher presenting the subject of elementary bacteriology. The exhaustion of the first edition has necessitated the issuing of a second edition. The most important change is to the more convenient octavo form.

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*Index-Catalogue of the Library of the Surgeon-General's Office, United States Army.* Authors and Subjects. Second Series. Vol. VI. G—Hernette. 1901. 4to. 1051 pages. Government Printing Office, Washington.

*A Manual of the Practice of Medicine.* By George Roe Lockwood, M. D. Second edition, revised. With 103 illustrations, many of them in colors. 1901. 8vo. 847 pages. W. B. Saunders and Company, Philadelphia and London.

*Diseases of the Intestines.* Their Special Pathology, Diagnosis and Treatment. By John C. Hemmeter, M. D., Philos. D. In Two Volumes. Volume I, Anatomy, Physiology, Intestinal Bacteria, Methods of Diagnosis, etc. With many original illustrations, some of which are in colors. 1901. 8vo. 742 pages. P. Blakiston's Son and Company, Philadelphia.

*Gynecological Pathology.* A Manual of Microscopic Technique and Diagnosis in Gynecological Practice. For students and Physicians. By Carl Abel. Translated and edited by Samuel Wyllis Bandler, M. D. With a Chapter on the Embryology of the Female Genitalia and the Pathological Growths Developing from Embryonal Structures. Illustrated by one hundred engravings. 1901. 4to. xv + 237 pages. William Wood & Company, New York.

*Nothnagel's Encyclopedia of Practical Medicine, Typhoid Fever and Typhus Fever.* By Dr. H. Curschmann. Edited, with additions, by William Osler, M. D. Authorized translation from the German, under the editorial supervision of Alfred Stengel, M. D. 1901. 8vo. 646 pages. W. B. Saunders and Company, Philadelphia and London.

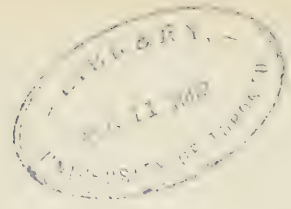
*Transactions of the Twenty-third Annual Meeting of the American Laryngological Association.* Held at New Haven, Conn., May 27th to 29th, 1901. 8vo. 274 pages. New York.

*Transactions of the Association of American Physicians.* Sixteenth Session held at Washington, D. C., April 30, and May 1, and 2, 1901. Volume XVI. 8vo. xxvii + 730 pages. 1901. Printed for the Association. Philadelphia.

*The Four Epochs of Woman's Life.* A Study in Hygiene. By Anna M. Galbraith, M. D. With an Introductory Note by John M. Musser, M. D. 1901. 8vo. 193 pages. W. B. Saunders and Company, Philadelphia and London.

*Transactions of the American Gynecological Society.* Volume 26. For the year 1901. 8vo. 406 pages. 1901. Philadelphia.

- A Text-Book of the Practice of Medicine.* By James M. Anders, M.D., Ph.D., LL.D. Illustrated. Fifth edition, thoroughly revised. 1901. 8vo. 1297 pages. W. B. Saunders and Company, Philadelphia and London.
- Nervous and Mental Diseases.* By Archibald Church, M.D. and Frederick Peterson, M.D. With 322 Illustrations. Third edition, thoroughly revised. 1901. 8vo. 869 pages. W. B. Saunders and Company, Philadelphia and London.
- The Pathology and Treatment of Sexual Impotence.* By Victor G. Veckl, M.D. Third edition, revised and enlarged. 1901. 12mo. 329 pages. W. B. Saunders and Company, Philadelphia and London.
- A Practical Guide to the Administration of Anæsthetics.* By R. J. Probyn-Williams, M.D. 1901. 12mo. 211 pages. Longmans, Green and Company, London, New York, and Bombay.
- The Roentgen Rays in Medicine and Surgery.* As an Aid in Diagnosis and as a Therapeutic Agent. Designed for the Use of Practitioners and Students. By Francis H. Williams, M.D. (Harv.) With three hundred and ninety-one illustrations. 1901. 8vo. xxx + 658 pages. The Macmillan Company, London, New York. Macmillan and Company, Ltd., London.
- Dose-Book and Manual of Prescription-Writing.* With a List of the Official Drugs and Preparations, and Many of the Newer Remedies with their Doses. By E. Q. Thornton, M.D., Ph.G. Second edition, revised and enlarged. 1901. 12mo. 362 pages. W. B. Saunders and Company, Philadelphia and London.
- Modern Obstetrics.* General and Operative. By W. A. Newman Dorland, A.M., M.D. With 201 illustrations. Second edition, revised and enlarged. 1901. 8vo. 797 pages. W. B. Saunders and Company, Philadelphia and London.
- A Text-Book of Diseases of Women.* By Charles B. Penrose, M.D., Ph.D. With 221 illustrations. Fourth edition, revised. 1901. 8vo. 539 pages. W. B. Saunders and Company, Philadelphia and London.
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- Outlines of Physiology.* By Edward Groves Jones, M.D. 107 illustrations. 1901. 12mo. 442 pages. P. Blakiston's Son & Company, Philadelphia.
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- Report of the Surgeon-General of the Army to the Secretary of War.* For the fiscal year ending June 30, 1901. 8vo. 354 pages. Government Printing Office, Washington.
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- A Laboratory Handbook of Urine Analysis and Physiological Chemistry.* By Charles G. L. Wolf, B.A., M.D. Illustrated. 1901. 8vo. 203 pages. W. B. Saunders & Company, Philadelphia and London.



# BULLETIN

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## A NEW METHOD OF PYLOROPLASTY.

By J. M. T. FINNEY, M. D.,

*Associate Professor of Surgery, Johns Hopkins University.*

The first plastic operation for the relief of a benign stricture of the pylorus was performed by Heineke in eighteen hundred and eighty-six. A few months later Mikulicz made use of exactly the same procedure, being at the time in ignorance of the work of Heineke. This operation has since borne the names of these two surgeons.

Before discussing the relative advantages and disadvantages of their particular method, a word or two, concerning other operative procedures designed to accomplish the same result, will not be out of place.

The methods used in the treatment of non-malignant stricture of the pylorus, seem, all of them, open to certain special objections. Digital or instrumental division of the pylorus, whether by the method of Loreta or Hahn, has proven very unsatisfactory as judged both by immediate risks and final results, and has been practically abandoned.

Jaboulay, in eighteen hundred and ninety-two, proposed the operation of gastroduodenostomy. Modifications of this method have been suggested by Duranti and Henle, but it has never met with much favor on the part of the profession. This operation I performed three years ago, in a case of pyloric stricture from old ulcer. The condition of the patient, an old lady, has been improved but not entirely

relieved. It was the partial failure in this case that led me to seek a better method.

The operation of pylorotomy, on account of the greater technical difficulties and increased danger in its performance, must of necessity remain of limited usefulness. Theoretically, of course, it is the ideal operation, but practically, except in rare instances, malignant disease is its sole indication.

Gastroenterostomy, devised by Nicoladoni in eighteen hundred and eighty-one, seems at the present time to be the operation of choice with the majority of surgeons, and the weight of surgical authority is decidedly in its favor.

But as to the relative merits or demerits of this operation, performed by whatever method, there still exists among surgeons, great diversity of opinion. Call it by whatever name you will, explain it as you may as being due to the reflux of bile into the stomach, or as resulting from the presence, in the duodenum, of particles of partially digested food, the fact remains that the "Circulus viciosus" of the Germans is present in a not inconsiderable percentage of cases, and when it does occur, it is productive of much discomfort to the patient, and is a grave menace to the success of the operation.

While it is undoubtedly true, that for some reason or

other, this percentage varies much in the hands of individual operators of large experience, still in the aggregate, the danger and suffering from this source are so great as to make it well worth while to eliminate it altogether, if it were possible. The great desideratum, of course, is to establish an opening between the stomach and bowel which will remain patulous and through which, at the same time, the bile and stomach contents will not tend to regurgitate.

From a careful study of the subject, it would seem that the Heineke-Mikulicz operation, while having in selected cases definite advantages over any other operation, still has certain recognized objections. Attempts to overcome these defects have been made by several operators. Richardson, of Boston, advocates an oval or diamond-shaped incision through the pylorus, which accomplishes the excision of the anterior portion of the stricture and leaves only the posterior wall as a hinge upon which the duodenum and stomach are brought together. Mayo Robson speaks with favor of this method, and Morrison has recently reported several cases in which he has made use of the same procedure with success. Koepelin and Jaboulay recommend what they call "sub-mucous pyloroplasty," in which the incision is carried down to but not through the mucosa. The divided serous, muscular and sub-mucous coats are then united in the usual way. They maintain that this modification is safer than the original method, the danger of sepsis being done away with. Enough cases, however, have not been reported to determine its usefulness, and it would seem, theoretically, at least, of doubtful utility. Mayo Robson advocates the use of an "internal splint in the shape of a bone bobbin over which to apply the sutures," a method, which, he states, has been employed in all his operations, and one which offers several advantages, for instance: "Only two continuous sutures are required, for the mucous and peritoneal margins respectively. The bone tube secures an immediate and thoroughly patent channel which affords protection for from twenty-four to forty-eight hours to the line of sutures, by which time union should be established. And it prevents the new channel being inadvertently made too narrow." This modification has been followed by other surgeons with success.

The operation which I propose is practically a modification of the method of lateral anastomosis suggested by Dr. Halsted. I have performed the operation five times. In all of my cases the pylorus was more or less adherent to the surrounding structures, abdominal wall, liver, gall bladder, omentum, and colon. In all the cases, the operation was carried out, notwithstanding the adhesions and thickened walls of the pylorus and stomach with entire satisfaction, and in four cases the result has been complete relief from all unfavorable symptoms. The fifth case has been operated upon too recently to judge as yet as to the result; but so far, he has been entirely relieved of his trouble, eats anything and is gaining steadily in weight. The operation is as follows:

Divide the adhesions binding the pylorus to the neighbor-

ing structures, also free as thoroughly as possible, the pyloric end of the stomach and first portion of the duodenum. Upon the thoroughness with which the pylorus, lower end of the stomach, and upper end of the duodenum, are freed, depends, in large measure, the success of the operation, and the ease and rapidity of its performance. I wish to emphasize this as one of the most important points in the operation. Frequently, at first sight, the pylorus may seem hopelessly bound down, when after a little patient toil and judicious use of the scalpel and blunt dissector, it is found that it can be freed with comparative ease. A suture, to be used as a retractor, is taken in the upper wall of the pylorus, which is then retracted upwards. A second suture is then inserted into the anterior wall of the stomach, and a third into the anterior wall of the duodenum, at equidistant points, say about 12 cm., from the suture just described in the pylorus. These second sutures mark the lower ends of the gastric and duodenal incisions, respectively. They should be placed as low as possible in order that the new pylorus may be amply large. Traction is then made upwards on the pyloric suture, and downwards in the same plane, on the gastric and duodenal sutures. This keeps the stomach and duodenal walls taut, and allows the placing of the sutures with greater facility than if the walls remained lax. See Fig. 1. The peritoneal surfaces of the duodenum and stomach, along its greater curvature, are then sutured together, as far posteriorly as possible. See Fig. 2. For this row I would recommend the use of the continuous suture, as it is more easily and quickly applied, and it can be reinforced after the stomach and duodenum have been incised. After the posterior line of sutures has been placed, an anterior row of mattress sutures is taken, which are not tied but left long, in the manner indicated in Fig. 3. These sutures, after they have been placed, are retracted vertically in either direction from the middle of the portion included in the row of sutures. See Fig. 4. Then after all the stitches have been placed and retracted, the incision is made in the shape of a horseshoe. The sutures should be placed far enough apart to give ample room for the incision. The gastric arm of the incision is made through the stomach wall just inside the lowest point of the line of sutures, and is carried up to and through the pylorus and around into the duodenum, down to the corresponding point on the duodenal side. Hemorrhage is then stopped. It is well to excise as much as possible of the scar tissue upon either side of the incision in order to limit, as far as possible, the subsequent contraction of the cicatrix. This procedure I carried out in two of my cases with great satisfaction, and I should strongly recommend it in all cases where the walls of the pylorus are much thickened and there is much scar tissue present. It is well, too, to trim off with scissors redundant edges of mucous membrane, in order to prevent the formation of a valve-like fold of mucous membrane at the new pylorus. A continuous catgut suture is now taken through and through all the coats of the intestine on the posterior side of the incision. See Fig. 5. This reinforces the posterior line of

sutures, secures better approximation of the cut edges of the mucous membrane, and prevents the reunion of the divided intestinal walls. The anterior sutures are then straightened out and tied, and the operation is complete, unless one wishes to reinforce the mattress sutures with a few Lembert stitches. See Fig. 6. This procedure, as is readily seen, gives the minimum of exposure of infected surface. All the stitches are placed and the posterior row tied, before the bowel is opened, and it remains open just long enough to control the hemorrhage. The size of the newly-formed pyloric opening is limited in this operation, only by the mobility of the stomach and duodenum, and the judgment of the operator. In all of my cases the incision has been about 12 cm. in length, and could have been made longer, had I chosen to make it so. Unless the stomach is very much dilated or has descended to an unusual extent, the lower limit of the new outlet is at or near the level of its most dependent portion.

When the stomach is much dilated, there is no contra-indication in this operation to the performance, at the same time, of gastropexy or gastroplication, if one considers them indicated.

In the matter of mortality, statistics, notoriously unreliable in cases of this sort, seem to slightly favor pyloroplasty as against gastroenterostomy. But, nevertheless, the latter operation numbers among its staunchest advocates some of the foremost names in the surgical world. Furthermore, it cannot be denied that during the past few years the operation of pyloroplasty has fallen somewhat into disfavor, partly because of the number of recurrences following it; and partly because of the improved methods recently introduced, and the increased facility in performing the operation of gastroenterostomy. Mechanical devices, such as the Murphy button and the bone bobbin of Mayo Robson, have contributed not a little to the accomplishment of this result. The range of usefulness of gastroenterostomy is, of course, much wider than that of pyloroplasty, which obviously must be restricted to cases of benign stricture of the pylorus. Although Morrison reports a case of early carcinoma of the pylorus treated in this way through mistaken diagnosis, with a result quite as satisfactory as that usually obtained by more radical methods.

The especial objections that have been urged against the Heineke-Mikulicz operation are:

- (1) Its inapplicability in cases of extensive and firm adhesions about the pylorus.
- (2) Its inapplicability in the presence of still active ulceration.
- (3) The liability to recurrence of the stricture due to contraction of the scar.
- (4) The inability to obtain good apposition on account of rigidity of the walls of the stomach and duodenum.
- (5) The outlet of the stomach is not placed at the most dependent portion, hence in the presence of motor insufficiency the aid of gravity in emptying the stomach is lost.

The effect of some of these objections to the operation is

lessened by the modifications suggested by Richardson, Morrison, and others, to which reference has already been made, but the validity of the others has been established by repeated observations.

I believe that all of these objections, with the possible exception of the second, viz: still active ulceration, are overcome by the method here suggested. I am convinced that adhesions, however firm or extensive, constitute no bar to this operation. With care and perseverance they can be separated. If the new pylorus is made sufficiently large, the danger of subsequent contraction is reduced to a minimum. Excision of the anterior portion of the thickened pylorus, and if necessary, the adjacent portions of the gastric and duodenal walls, lessens materially the danger of subsequent contraction, and at the same time allows of easy approximation of the two surfaces.

In an extremely interesting monograph by Carle and Fantino, the functional results following the operations of gastroenterostomy and pyloroplasty are compared. Robson summarizes their findings briefly as follows:

"Points in favor of pyloroplasty:

- (1) Regurgitation of bile into the stomach is prevented.
- (2) Secretion of hydrochloric acid, when it has been excessive, becomes normal.
- (3) If the secretion of hydrochloric acid has been diminished or absent before the operation, it remains in statu quo after operation.
- (4) If there has been primary gastric atony, peristalsis is but little improved.
- (5) This function improves rapidly or reaches perfection if the muscular contractility has been normal or increased, and when the obstruction was due to fibrous stenosis or pyloric spasm.
- (6) In all such cases evacuation of the stomach is accomplished in its physiological period. Only in rare cases, and these only in the first months after operation, may it be delayed.

(7) The capacity of the stomach always decreases, but rarely becomes as small as normal.

(8) The pylorus recovers tone.

Points of difference between the results of pyloroplasty and gastroenterostomy:

- (1) The absence of regurgitation of bile, and hence the absence of any biliary influence on the gastric secretions.
- (2) The evacuation of the stomach is not accelerated; hence the difficulty the stomach has in reaching its normal size.
- (3) The slight or negative result obtained by pyloroplasty in obstruction from primary gastric atony compared to the positive results from posterior gastroenterostomy."

A word as to the preparation of patients for this operation. Accumulated clinical experience has proven that it is unnecessary and often harmful, to put patients through a long course of preliminary treatment. The observations of Cushing in the Johns Hopkins Hospital, upon the bacteriological examination of the stomach contents, show that

cleansing the mouth and teeth carefully with antiseptic washes and the administration of sterile food only, will quickly render the stomach contents innocuous. The treatment carried out in all of my cases was as follows:

For two or three days before the operation the mouth and teeth were carefully cleansed with carbolic solution and only sterile liquid food and water administered. The stomach was irrigated night and morning, just before operation, with boiled water. No food at all was given by mouth for the twelve hours preceding operation. Cultures were taken from the stomach contents in three of the cases and two were found to be sterile. The skin preparation is the same as for all abdominal cases. I prefer the incision through the right rectus muscle, and make it sufficiently long to give abundant room, say six to eight inches. The greatest care is exercised in protecting the abdominal cavity from soiling by extravasated stomach contents, by the liberal use of Mikulicz' pads of sterile gauze. In two cases Schleich's solution and one per cent solution of cocaine were made use of, but ether had to be substituted in small quantity toward the close of the operation. The abdominal wound is closed without drainage. Nothing is given by mouth for the first thirty-six to forty-eight hours. Enemata of salt solution and coffee are given every five hours, for the first twenty-four hours, after which time nutritive enemata are alternated with the salt solution. Water in small quantities is allowed early. On the second or third day albumin in teaspoonful doses is administered, and if borne well, broths and milk are rapidly added.

Patients, particularly weak ones, are not required to lie flat on the back, but are encouraged to turn and even allowed to be propped up in bed very soon after the operation.

*Case I.*—Miss Emily P., referred to me by Dr. Dunott, of Baltimore, a student, aged twenty-one, entered the Union Protestant Infirmary February 23, 1901, complaining of "stomach trouble." Her family history is negative. She had always been healthy until her present illness began two and one-half years ago as an attack of indigestion which culminated in a severe attack of nausea and vomiting which lasted for some days. Since that time she has always had more or less abdominal distress, has seen many physicians, with little or no relief.

Her attacks seemed at times to be aggravated by partaking of food; at other times, not.

Vomiting was copious and severe; nausea almost constant. She has never vomited blood except after the use of the stomach tube.

Has lost about fifteen pounds recently, looks pale, anæmic, and somewhat emaciated.

Heart and lungs normal. Abdomen slightly distended. Stomach tympany greatly increased. Succussion pronounced. Palpation negative except slight tenderness and muscle spasm over the right hypochondrium.

Patient had been operated upon about three months pre-

viously by Dr. Dunott. The abdomen had been opened, some induration was found about the pylorus, the gall bladder was adherent to it. There was a scar, apparently of an old ulcer, in the anterior wall of the stomach near the pylorus and the anterior wall of the pylorus was folded upon itself, making a partial stricture.

The adhesions were separated, and the pyloric wall unfolded as much as possible, when the stricture of the pylorus seemed to be relieved. The stomach was not opened. There was a second scar, also, in the anterior wall of the stomach near the pylorus. Her abdominal wound was closed without drainage. She made a good recovery from the operation, but experienced little or no benefit from it and returned, as before stated, about three months later, for a radical operation.

On opening the abdomen, it was found that the omentum was very adherent to the pylorus and to the scar of the previous operation. The gall bladder was also very firmly adherent to the pylorus and duodenum. The stomach was found to be greatly dilated and scars of old ulcers were apparent near the pylorus. The pylorus, itself, was found much thickened. After freeing all the adhesions, an anastomosis between the stomach and duodenum was accomplished. The pylorus was found to be much contracted, the orifice being less than 1 cm. in diameter.

She made an excellent recovery and reported a few days ago that since the operation, she has been absolutely free from any of her former trouble. At an examination, a few weeks ago, the stomach had diminished to about the normal size. She has gained markedly in weight.

*Case II.*—Mrs. Anna S., aged fifty-five, entered the Union Protestant Infirmary March 16, 1901, referred to me by Dr. J. Friedenwald, of Baltimore, complaining of indigestion and "stomach trouble."

Family history negative. Her trouble dates back about a year. Symptoms have been very severe for about six months past, during which time nausea, vomiting, constipation, and loss of weight have been very pronounced.

She has never vomited blood. Has been unable to eat anything but liquid food, milk, and crackers. Vomits frequently large quantities. Her only relief is from the daily use of the stomach tube. She has lost forty pounds in the last six months.

Examination of the patient shows an exceedingly emaciated, somewhat anæmic looking woman. Heart and lungs negative. Abdomen considerably enlarged. Liver dullness normal. Stomach tympany much increased.

Muscle spasm and tenderness on palpation over the pylorus, otherwise negative.

Dr. Friedenwald had the patient under observation for some time and examined the stomach contents repeatedly. There was marked hyperacidity. On March 19, the abdomen was opened in the usual way and a number of adhesions were found about the pylorus, which was fairly movable. After freeing the adhesions, this operation was carried out

very satisfactorily. The patient, although not in very good condition at the time, stood the operation very well, and made a rapid and complete recovery.

I saw her a few days ago; she had regained her forty pounds and was looking the picture of health. She said she ate anything and everything and digested it with no difficulty.

*Case III.*—Mary M., aged twenty-eight, entered the Johns Hopkins Hospital April 12, 1901, referred to me by Dr. J. Friedenwald, of Baltimore, complaining of "stomach trouble."

Family history negative, no tuberculosis or cancer. History of trouble dates back twelve years, during which time she has suffered always more or less after eating. No appetite. Very constipated. No history of injury.

Her chief complaint is distress after eating, occasional attacks of bloating of stomach and vomiting with pain. Epigastric distress increased by food, relieved by vomiting. Pain radiates to back and right side. Two years ago had severe hemorrhage. Vomitus occasionally suggests coffee grounds. Has lost thirty pounds in weight. Is very weak, and for the last two years has lived on milk, soup, and crackers. She has used the stomach tube for the past year daily.

Patient is very pale, thin, and anæmic looking. Heart and lungs normal. Abdomen not distended, slight tenderness over epigastrium.

Area of gastric tympany increased. Liver dullness normal. Palpation negative.

She had been in the Johns Hopkins Hospital two years previously when an exploratory laparotomy had been performed by Dr. Halsted.

The organs all seemed normal at that time, no thickening about the pylorus. A longitudinal incision was made in the anterior wall of the stomach near the pylorus through which the mucous membrane was examined and no lesion found. No apparent contraction of the pylorus. Stomach wound was closed, no drainage.

She was relieved of her symptoms for about one year. Eighteen months later she entered my service at the Union Protestant Infirmary. Her condition at that time was about the same as before the operation. I opened the abdomen expecting to do a gastroenterostomy. I found many adhesions about the pylorus and lower end of the stomach which doubled it in upon itself and decreased the lumen markedly. After these adhesions had all been separated, I invaginated the anterior wall of the stomach on my finger and passed it through the pylorus which seemed about the normal size. I could dilate it easily. The stomach not being noticeably enlarged, it seemed as if the development of adhesions after Dr. Halsted's operation had been responsible for the return of the trouble. I, therefore, having stretched the pylorus thoroughly with my finger, after the method of Hahn, closed the abdominal wound without drainage.

She was again relieved of her symptoms, but only for a few months, and reentered the Johns Hopkins Hospital on April

12, 1901, for a radical operation. Her condition at that time has been described. On opening the abdomen a great mass of adhesions was encountered, binding together the liver, stomach, duodenum, omentum, and parietal peritoneum. Considerable time was consumed in separating these adhesions during which hemorrhage was quite free but easily controlled by pressure and ligature. The pylorus was bound up in adhesions to the omentum, gall bladder, and liver. The left lobe of the liver was thinned and very adherent to the anterior surface of the stomach. The pylorus was quite indurated and thickened. The stomach was considerably dilated.

After freeing all the adhesions, the stomach and duodenum were brought together, and an anastomosis established between them in the manner described.

Notwithstanding the many and dense adhesions and the thickness of the walls of the pylorus, the operation, once the adhesions had been separated, was accomplished without further difficulty.

She made a good recovery and is now completely relieved of her trouble. I saw her a few days ago, and she had gained about forty pounds, and says she eats and digests anything she wishes.

*Case IV.*—J. M. B., referred to me by Dr. J. Friedenwald, of Baltimore; aged forty-eight, barkeeper; admitted to the Johns Hopkins Hospital March 18, 1902, with the history of "stomach trouble" for years, also that a piece of stomach tube had broken off in the stomach during the act of washing out.

Family history negative, no tuberculosis, no cancer. Patient has had the usual diseases of childhood, typhoid fever, pneumonia, very subject to cold, has had a cough, now, for four years. Has been a very hard drinker. The patient gives the history of having had indigestion and "stomach trouble" for twenty years. Began with pain and vomiting after eating. Has been very severe at times, radiating to back and right shoulder blade. Eighteen years ago had severe hemorrhage from stomach. He has had a great deal of trouble ever since this time, frequently vomiting food that has been in his stomach for several days. He has been under treatment during most of the time, having consulted many physicians. Bowels irregular.

About three years ago, by the advice of his physician, he began the use of the stomach tube, but discontinued it after a time. Eleven days ago, while using an old tube, that he had had for five years, it broke and more than half of it remained in the stomach. The patient insists, that during the time this piece of tube has remained in his stomach, he has been feeling better than for years past.

Examination of the patient shows an extremely pale and emaciated man. In the chest there are indications at both apices of beginning tubercular trouble. Heart negative. Abdomen rather full, considering the extreme emaciation; liver dullness about normal. Stomach tympany extends over 1 cm. below the umbilicus, and well beyond the middle line.

Palpation of the abdomen negative. No movable dullness detected. Marked edema of both legs. Finger nails markedly clubbed.

On March 19, abdomen was opened under Schleich's solution anesthesia, after preliminary hypodermic injections at hour intervals, of one-sixth of a grain each of morphia, hypodermically. There was considerable ascitic fluid in the peritoneal cavity.

The stomach was found to be much enlarged and displaced downward. Liver about normal in size, rather hard, with some scar tissue over the pylorus. Gall bladder slightly distended but not adherent. The pylorus was very much scarred and puckered. Its walls much thickened and indurated. It was very adherent to the liver and transverse colon.

The omentum was tightly bound to it in several places. The pylorus itself was so firmly fixed by the adhesions from below, that it was possible to raise it but slightly. The duodenum was adherent near the pylorus but free below. It was found possible to oppose the stomach and duodenum after freeing the adhesions about the pylorus. The operation of pyloroplasty was then performed in the way already described. It differed only in that the incision was made considerably longer, about 15 cm. in length. The dense scar tissue in the anterior wall of the pylorus, and the neighboring portion of the stomach was excised. The wall of the stomach at this point was very dense and firm and over 1 cm. in thickness. A portion of stomach tube about 35 cm. long was found in the stomach and removed.

There was no difficulty in applying the sutures, and the operation was carried out with great facility. The whole procedure occupied about fifty minutes.

The patient stood the operation well, and up to the present time (3 months) has been doing uninterruptedly well.

*Case V.*—J. A. W., aged twenty-two, referred to me by Dr. L. P. Hamburger, of Baltimore; a farmer by occupation; admitted to the Union Protestant Infirmary May 23, 1902.

Complains of burning and a sense of weight in the stomach. Several paternal aunts were afflicted with consumption. No history of tumor. Does not use alcohol or tobacco.

Present illness began three and a half years ago with la grippe. Following this illness, he was left weak. During the summer of 1898, he belched much and regurgitated his food. Up to November of 1898, lost about ten pounds. At this period, he gave up work because of weakness and a "pulling" sensation in the abdomen. The winter of 1898-99, he spent in the Maryland General Hospital and has gone the rounds of hospitals and doctors ever since, without improvement. In the spring of 1898 weighed one hundred and forty pounds, and in the spring of 1899 weighed one hundred and five pounds. Because of the burning sensation in the abdomen, he has been obliged to limit his diet since 1899 to eggs, milk, cocoa, and toast. Complaint has continued off and on in varying intensity ever

since. In addition, he is compelled to expectorate saliva almost continually. Has never vomited blood.

He is worse in the summer, and there is a slight improvement in the winter. His average weight now is one hundred and twenty-seven pounds. His appetite is good, but any increase in his diet causes diarrhea.

On physical examination, patient is very poorly nourished, tongue lightly furred, mucous membranes fairly good color. Patient blushes readily.

Heart and lungs clear. Temperature 99°. Abdomen looks natural. Distinct clapotage in the left hypochondrium. The right kidney is distinctly palpable. Outline of stomach tympany on inflation from left nipple to 3 cm. below umbilicus.

An Ewald test meal showed free hydrochloric acid, no lactic acid.

On May 30, 1902, I performed the operation of pyloroplasty by the method described. On opening the abdomen, the stomach was found to be slightly dilated and its walls quite flabby. At the pylorus, on the anterior wall, was the puckered scar of an old ulcer. The pylorus would not admit the tip of the index finger. Posteriorly, there were some adhesions between the stomach and duodenum. When these had been thoroughly freed and the scar tissue in the anterior wall of the stomach had been excised, the operation as described was performed.

The appendix was found very long and bound down by adhesions on the anterior surface of the ascending colon. As the tip of the appendix was adherent to the gall bladder, the appendix was excised.

The patient has made an excellent recovery and at the present time, one month after the operation, has gained several pounds. He is eating and digesting regular hospital diet, and expresses himself as very much relieved.

From my study of the other methods suggested for the relief of benign stricture of the pylorus, and from my experience in the foregoing cases, I believe the following conclusions are justified:

(1) All the operations heretofore suggested for the relief of benign stricture of the pylorus are open to serious individual objections.

(2) The operative procedure made use of in the cases here reported combines more good points and less objectionable features than any other method that has been suggested up to the present time.

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FIG. 1.



FIG. 4.



FIG. 2.

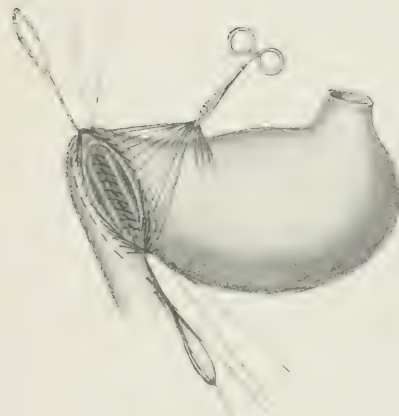


FIG. 5.

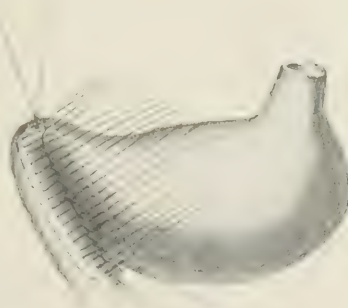


FIG. 3.



FIG. 6.



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## THE SURGICAL TREATMENT OF TUBERCULOUS CERVICAL ADENITIS.

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This communication is based on the study of 170 cases of tuberculous disease of the lymphatic glands of the neck, treated in the service of Dr. Halsted in the Johns Hopkins Hospital between August, 1889, and February, 1902.

An effort has been made to examine the patients personally, or to communicate with them or their physicians by letter. Owing to the frequency of the affection in the colored race and in the lower classes in general, individuals whose residence is constantly changing, the cases have proved unusually difficult to follow and a very large number have to be recorded as lost.

Especial attention has been paid to the complications and remote affections after the operation and to the condition of the lungs, and a comparison made between our findings and the statistics given in recent literature. Articles by Blos, Jordan, and others have been freely drawn upon, although no attempt has been made to review the enormous literature of this subject. Many of the earlier histories are incomplete in details, especially in the examination of the lungs. Of the 170 cases, 27, for various reasons, did not receive truly surgical treatment, or the records were too incomplete to be of service. These will, therefore, not be considered in discussing the results, thus leaving 143 upon which our statements are based.

*Frequency.—Race, Sex, Age.*—Of 13,000 surgical patients, 1098 were admitted for tuberculosis, and of these, 170 with tuberculous glands of the neck; that is, 8% of all the surgical patients were admitted for tuberculosis, and 1.3% of all for tuberculous glands of the neck. The neck cases comprise 15% of all those with tuberculosis, and are exceeded in number only by those with hip-joint disease. Of whites there were 83 cases; of negroes 61, that is about 4 to 3. The average ratio of whites to negroes in the hospital is 7 to 1, so that it is evident that the disease is more prevalent among the negroes. Like all tuberculous affections, it is found where hygienic conditions are poorest, 82% living in the city, 18% coming from the country or small towns. Males outnumber females as 3 to 2. The youngest was 18 months, the oldest 66 years of age. The average age

is somewhat younger in females. Between 10 and 30 there occur 76%. This corresponds exactly to the statistics of Fuernrohr in Erlangen. Tabulation according to decades gives the following:

Age....	1-10	10-20	20-30	30-40	40-50	50-70
Cases..	16	36	54	8	7	2

These ages are taken at the time of admission for treatment and, according to Blos, do not represent the true beginning of the disease, but rather the time at which a latent infection begins to develop, that is about and after puberty. Volland noted that in the Swiss schools 96.6% of children between 7 and 9 years of age had enlarged cervical glands; this high percentage gradually decreasing until puberty. To this condition the term *scrofula*, if used at all, should be restricted; that is, a chronic hyperplasia, gradually decreasing as puberty is approached. Such swollen glands offer conditions most favorable to tuberculous infection, and it is possible that the infection may take place at this time, and remain latent until after puberty.

*Duration.*—The duration of the disease before admission, as noted by the patients, varied from 1 week to 20 years in our cases.

Months...	0-2	2-4	4-6	6-8	8-10	10-12				
Years....							1-5	5-10	10-15	15-20 20-
Cases....	9	13	10	14	3	4	52	13	2	2 1

Many give a history of fluctuation in the size of the glands, and in some the swelling has at times entirely subsided to reappear in the course of months or years.

*Etiology, Infection, Heredity.*—As to the source of infection our histories show little; apparently this point was not well considered in the examination of the patients. Four followed la grippe, three diphtheria, one coryza, bronchitis, or catarrh, and one was attributed to a blow in the neck, while one followed pediculosis capitis. About one-half give a family history of tuberculosis. This is much larger than the proportion given by Blos, 28% in 851 cases. It is ordinarily stated that one-third give an hereditary history. The disease was formerly thought to be a local manifestation of a general infection. The opinion at the present time is that

it is as a rule primarily local. The infection is evidently a descending one and various parts of the pharynx are assigned as portals of entry, of which the tonsil is the most common, an hypertrophied tonsil especially offering favorable conditions for infection. There is not necessarily a tuberculous lesion at the point of entrance. Nicoll has found tubercle bacilli in tonsils and adenoids when there was no tuberculous lesion here or elsewhere. Carious teeth may also be a starting point, and Stark has demonstrated tubercle bacilli about their roots. The disease sometimes follows acute exanthemata and some cases can be attributed to diseases of the skin about the face or head. Cervical glands comprise about 90% of all tuberculous glands. This is probably explained by the fact that the glands of the neck, owing to the area which they drain, are especially subject to inflammatory swelling in childhood, and such hyperplastic glands offer favorable ground for tuberculous infection.

*Glandular Involvement.*—The distribution of the glands affected speaks strongly in favor of a descending infection, 70% being in the superior triangle, and where all the triangles are involved, the disease is generally more extensive in the upper portion of the neck. The glands of the neck may be roughly divided into four groups; those in the anterior triangle and those in the posterior, with two connecting chains, one passing in front, the other behind, the sternomastoid muscle. The connecting chain behind the muscle seems to be the one most commonly involved, a fact which accounts for much of the difficulty of operation. The right and left sides of the neck are affected with about the same frequency, and fully one-half the cases have involvement of both sides. The axilla is often secondarily involved, seven times in our list. Axillary infections are probably always secondary to infection of the neck, unless there is some definite tuberculous lesion, as of the ribs or fingers, in the region which these glands drain. In only two cases was there also involvement of the glands of the groin or the popliteal space. One case had been operated upon previously for tuberculous peritonitis, one for lumbar abscess, and one had a previous history of tubercular meningitis, one of tuberculosis of the dorsal vertebrae, one of tuberculosis of the knee.

*Condition of the Lungs.*—In 34 cases there was no note on the condition of the lungs before operation; 89 were stated as being negative; 13 as suspicious, and 7 showed positive evidence of tuberculosis. Taking together those cases in which the lungs were definitely tuberculous or in which there was a suspicion of tuberculous infection, there are 14%, while only 4.9% showed positive evidence of tuberculosis. In various statistics these percentages differ widely, thus Fraenkel states that lung involvement is present in about 10.2%, while Jordan had 26%. An average of five different statistics would show about 19% of cases with affection of the lungs. According to Blos, tuberculosis of the glands of the neck serves as a frequent source of infection for the lungs, the course of the infection being either through the lymphatics or the blood.

*Pathology.*—The glands differ widely in their appearance and in the same neck may show all degrees of involvement. According to Jordan, they may be divided into four groups, all of which are stages of the same process, and all of which may be found existing together. The simplest of these forms is pure hyperplasia. Here there is a general enlargement of the glands of the neck without the formation of any nodes, the glands on section showing a homogeneous structure and their true nature being disclosed only by the demonstration of tubercle bacilli. There is nothing macroscopically or microscopically pathognomonic. The bacilli are very few in number and their presence can often be demonstrated only by animal inoculation.

The second type is characterized by the formation of nodes. On section one sees scattered over a gray or grayish-red background fine lighter grayish points, which under the microscope are shown to be typical tubercles. The size of the nodes varies from that of a pea to an egg, all presenting on section the same appearance.

The third type is characterized by caseation. The tubercles have increased in number and the gland has undergone retrograde metamorphoses. The whole gland may be converted into a caseous mass and even the smallest ones may show the same structure. The gland may be entirely broken down and converted into an abscess bounded by its capsule.

In the fourth group the inflammation has spread to the periphery and involved the gland capsule and the periglandular structures. There is new formation of connective tissue, binding together neighboring glands and surrounding structures, skin, muscle, etc. The glands may have completely broken down and coalesced to form a large cyst filled with pus and caseous matter. In one case we had such a cyst extending from the mastoid process to the spine of the scapula 7 cm. below the clavicle. The skin may become involved and eventually the abscess burst and ulcers and discharging fistulae result. These forms may be all combined, and in addition there may be a pyogenic infection which can lead by abscess formation to actual cure of the tuberculous process in any stage. There may also be a calcareous deposit, or a tuberculous process may be encapsulated in connective tissue and remain quiescent or subject to exacerbations.

*Symptoms.*—The clinical picture is usually a characteristic one. The patient, ordinarily a young person, presents himself with a tumor of varying size, situated, or at any rate most prominent, in the upper part of the neck, with perhaps scars of old abscesses or possibly the presence of ulcers and fistulae. There may be slight fever, although as a rule it is absent. Pain also is usually wanting, although sometimes, if the tumor is large, there may be pain from pressure on the cervical nerves. There is often slight anemia, the hemoglobin varying from 70% to 80%. There may be some loss of weight.

*Diagnosis.*—The diagnosis is generally easy. At times it may be difficult to distinguish from actinomycosis, syphilis, lymphosarcoma, Hodgkin's disease, carcinoma, cysts, or

chronic hyperplasia. Most of these affections can be ruled out by the character of the tumor or the presence of other manifestations of disease. The removal and microscopical examination of a gland will generally settle the question if there is any doubt. Too much emphasis cannot be laid on the tuberculin test. We have records of 25 cases in which tuberculin has been given to patients suffering from tuberculous cervical adenitis, and one in which Koch's lymph was given. In this last case the patient was reported discharged well four weeks after the last injection and there is no further note, the patient being subsequently lost sight of. This case is interesting inasmuch as general tuberculosis followed in two cases of tuberculous arthritis in which Koch's lymph was given. The tuberculin used was made by Dr. Trudeau, and reaction followed in all but one of the 25 cases. In this case a note on the history states that the same sample of tuberculin gave no reaction in several other cases which were known to be tuberculous. It may possibly be explained by the dose being too small, or there being some error in its administration. As tubercle bacilli had been demonstrated in the sputum, it was undoubtedly a case of tuberculosis. In all of the cases but one in which there was a reaction there was evidence of tuberculous disease found at operation. This patient was discharged not treated after a positive tuberculin reaction. Twenty of the 25 patients reacted to the first injection. The average time before the temperature rose was about 8 hours; the duration of the reaction following about 30 hours. The temperature ranged somewhat higher than is common in tuberculosis of other organs of the body. In 9 cases it was above  $102^{\circ}$ ; in one case it reached  $105.5^{\circ}$ . General symptoms, such as headache, loss of appetite and general discomfort, were common. Local symptoms were observed in comparatively few cases. In a number of cases in which it was difficult to say whether the patient was suffering from some form of cyst or from tuberculosis, and in all cases of Hodgkin's disease, tuberculin was given. There was no reaction in any but tuberculous cases, and in no case have we seen any ill effects from its administration.

*Prognosis.*—The outlook depends upon the form, stage, etc., of the disease and on the complications, especially tuberculosis of the lungs. Tuberculous gland disease is seldom in itself fatal. The prognosis is worse in children, and improves with age. It is worse where there is a history of heredity, and the outlook is necessarily more grave where there have been recurrences. Tuberculosis of the neck in general is one of the forms of tuberculosis which remains longest local. Spontaneous healing is possible in all stages by encapsulation or by the formation and rupture of an abscess, as is strikingly demonstrated by the large number of persons one meets on the street, with ugly contracting or keloidal scars in the neck. This, however, should not be counted upon; and the tuberculous focus is always a danger to the organism as a point from which tuberculosis may

spread. In 16 of 308 cases of Blos there was spontaneous cure without any interference.

*Treatment.*—Treatment may be constitutional, by local applications, or by operative procedure.

*Constitutional treatment* consists in attention to hygienic surroundings and improvement of the general condition by life in the open air, sea bathing, or the administration of tonics, cod liver oil, creosote, etc.; and whether local applications or operative procedures are resorted to, constitutional treatment should be recommended both before and after. In a recent report from Guy's Hospital, Dr. Harnett emphasizes the importance of hygienic measures and thinks that operative procedures are too often resorted to and are much too extensive. If the glands have not become very large and are not broken down and have existed for less than two years, hygienic measures, he thinks, should be first tried, and provided these are carried out and continued for long periods there is no doubt that in a large proportion resolution will occur. If, on the other hand, the disease has existed for over two years and the glands have attained considerable size, he advises the removal of the enlarged glands by enucleation through numerous transverse incisions. He bases his remarks on 200 cases, although his results are not stated. Undoubtedly many cases, especially those in the stage of simple hyperplasia, will entirely subside under constitutional treatment alone.

*Local treatment* consists in the application or injection of various substances, as iodine. Of our cases 28, afterwards operated upon, had been previously treated by the application of iodine locally, or by injections of iodine or iodoform, sometimes combined with incision, or by the rubbing in of various ointments. This latter practice cannot be too strongly condemned as it can only serve to encourage inflammation about the glands, and we have never seen any permanent good results from local treatment in any form.

*Operative procedure* may be conservative or radical.

*Conservative treatment* consists of simple incision and curettement with the application of iodoform, or of partial excision of the glands, that is removal of those glands which are seen to be definitely tuberculous. Simple incision is to be recommended only as a measure preliminary to the later radical operation, although many cases have gotten well with no other treatment. Twelve cases have been so treated, in all of which iodoform was applied at the time of operation. Where a single gland is involved, which is most common in the submaxillary region, results from this procedure have been very satisfactory, iodoform apparently having a certain retarding effect on the tuberculous process. Partial excision, or removal of the involved glands only, has been resorted to in 69 cases.

*Radical operation*, that is removal of all the glands with the surrounding fat, has been done in 59 cases. The operation of complete excision of the glands of the neck may be extremely difficult, especially where there is sinus formation or suppuration with extensive periglandular adhesions. The selection of an incision admits of much choice and numerous

methods have been recommended with a view to getting the best exposure with the least resulting scar. The operation as usually done in this hospital is as follows: A long incision is made beginning behind the ear over the mastoid process, curving forward over the edge of the sternomastoid muscle, and then slightly backward to the middle of the clavicle. A transverse incision is then made along the clavicle, forming a T. The skin is now dissected back, giving a large quadrilateral exposure, through which all parts of the neck can be easily reached, even the submental region. The dissection is now begun in the angle between the posterior border of the sternomastoid muscle and the clavicle. The subcutaneous fascia and platysma muscle are divided and turned back and a few posterior fibres of the sternomastoid severed, thus exposing first the external jugular vein. This is divided and ligated and brings one directly to the omohyoid muscle, which serves as a key to the operation. The omohyoid is seized with two clamps and cut, and becomes an excellent retractor and guide. By following it the internal jugular vein is readily exposed in spite of any amount of adhesions. Using the omohyoid as a retractor, the sternomastoid is pulled aside and the dissection carried up along the internal jugular vein and the posterior border of the sternomastoid until the posterior branch of the spinal accessory nerve is encountered. This is dissected out of the mass of glands, and the glands delivered beneath it. The whole dissection is thus carried from below and from the middle line upwards and outwards. By following these steps the operation is greatly simplified and a great advantage is that the internal jugular vein is exposed in its lowest portion at the very beginning of the operation. A provisional ligature can be passed around it and if the vein is later injured above, the entrance of air is readily prevented. The most difficult stage of the operation is reached in the upper part of the neck. The chain of glands which is always involved, and usually most extensively involved, is that group connecting the anterior and posterior triangles behind the sternomastoid muscle. Through the midst of these glands the spinal accessory nerve passes and it is often so intimately adherent to the mass of glands that its separation involves most difficult dissection. The greatest care should be exercised in leaving this nerve uninjured, as from it comes the supply to the sternocleidomastoid and trapezius muscles. These glands being freed, are delivered beneath the spinal accessory nerve and sternomastoid muscle, and with the glands from the lower portion of the neck are dissected upwards and outwards from the underlying structures. It is impossible in this dissection to avoid the cervical plexus and many branches of these nerves are divided. In mild cases many of them can be saved. The descendens noni is never necessary. When there is involvement of the sternomastoid muscle, removal of a portion or all of the muscle is indicated, and at times a portion of the trapezius also. If there is extensive periglandular inflammation and if the

tuberculous process has spread beyond the glands and periglandular fat, it is sometimes impossible to save the spinal accessory nerve and the operation is made much less difficult and its duration shortened by hours by the following procedure: Following the omohyoid muscle as a guide, the sternomastoid is divided immediately after division of the omohyoid by using the omohyoid as a retractor and cutting across the sternomastoid low down in the neck on top of the omohyoid. In this way there is no danger of injuring the vessels and the division of the sternomastoid can be easily accomplished. The omohyoid passes beneath the sternomastoid below that point where the posterior branch of the spinal accessory nerve leaves the muscle, and this posterior branch having been freed, it may practically always be saved even after division of the muscle. The operation in these cases proceeds as follows: Having divided the omohyoid and the sternomastoid, the sternomastoid is reflected in both directions, exposing the whole of the region lying beneath it and leaving the anterior and posterior glands connected by the mass of glands lying beneath the sternomastoid muscle close against the mastoid process. It is possible and comparatively easy with this exposure to still preserve the spinal accessory in its upper portion, that is the portion supplying the sternomastoid muscle, although a sacrifice of the posterior branch may in rare cases be necessary. In all of our recent cases we have been able to save the nerve in both branches after division of the muscle. The internal jugular vein if involved in the process should be ligated and removed. This involves no difficulty and is followed by no ill effects and is advised in all cases by Watson Cheyne and others if the freeing of the vein is very difficult and there is danger of much hemorrhage from its branches. The glands and surrounding fat having been thoroughly removed, the sternomastoid and omohyoid muscles are sutured with catgut. The skin is then closed with subcutaneous silver sutures and a rubber protective drain is placed through a buttonhole in the outer flap of skin, which is the most dependent part of the wound for the first twenty-four hours. This drain never causes any trouble and is removed at the first dressing at the end of a week or ten days. It is a great safeguard and prevents that filling of the wound with serum which is so apt to occur and which may prevent primary healing. The neck is fixed by a large dressing of gauze and plaster of Paris, reinforced by thin basswood splints and embracing the head and shoulders. The patients are allowed to sit up on the day following the operation and to walk about the ward within twenty-four hours. The division of the sternomastoid muscle and the spinal accessory nerve is to be most carefully avoided whenever possible; but in very adherent cases, if there is sinus formation, it is impossible to thoroughly remove the glands without dividing the muscle and possibly injuring the nerve, and the resulting deformity is so slight that it is not noticed by the patient unless his attention is called to it. The advantages of free exposure are only to be appreciated after operating upon a number

of adherent cases. The resulting scar is in most cases slight, although it shows above the collar and, being in the perpendicular direction, is more apt to spread than are transverse incisions. The incision used here is much the same as that used by Watson Cheyne. Harnett, with a view to avoiding the spreading of a perpendicular scar, advises several transverse incisions with the removal through each, of those glands which can be reached, but it hard to believe that a thorough removal can be done through such incisions. The incision recommended by Dowd, and previously by Baetson of Glasgow, begins in the anterior triangle beneath the jaw, runs back just beyond the hair line, down within the hair line to the lower portion of the neck, and then forward along the clavicle, turning forward a large skin flap. It has the advantage of leaving the perpendicular portion of the scar to be covered with hair and the transverse portions hidden above in the fold of the neck beneath the jaw and below by the collar. Whatever incision is used, however, the first object should be to obtain a free exposure of the whole side of the neck, and in severe cases where there is sinus formation the incision has to be modified according to the location of sinuses. While cosmetic considerations should always be borne in mind, complete removal of the glands is the first point to be thought of, and the incision should be made with a view to this rather than with fear of the resulting scar. One can always count upon the glandular involvement being much more extensive than it appears from external examination and the incision should be made with this in mind. A case in which the glands appear externally as a small mass in the upper part of the neck is apt to show at operation a chain of involved glands along the internal jugular vein which may extend all the way to the clavicle. The above incision has been found most satisfactory in 60 cases of tuberculous cervical adenitis operated upon by the writer in the last three years and in many cases of Hodgkin's disease or carcinoma or sarcoma of the cervical glands.

*Complications and Immediate Results.*—The dangers of the operation are slight and its mortality practically zero. In the 328 cases reported by Blos in Heidelberg there were no deaths, although the operations were done for the most part by younger assistants. In 10 statistics collected by him there were only three in which there was death from operation. Occasionally we have seen tachycardia for a few days. Shock is extremely rare. There is little hæmorrhage after the skin is reflected and if the internal jugular vein is exposed in its lower part early in the operation, there is no danger from its injury, as hæmorrhage from it can be easily controlled by pressure with the finger until the vessel is secured. In early cases in which this precaution was not observed there were twice alarming symptoms from entrance of air, the patients becoming cyanosed, with rapid respirations, and the pulse rapid and intermittent. In both of these, however, the symptoms soon passed off. The internal jugular vein has been many times removed, and in a few cases the carotid artery also, with no ill effects.

On the left side of the neck the *thoracic duct* must be considered, extending as it does often a couple of centimetres above the clavicle. Injury of the duct, however, does not seem to be the serious matter it was formerly thought. The duct has been injured four times in our series of cases. In the first of these the wound was a longitudinal tear. An attempt was made to suture it and a drain was placed leading to the duct. The suture, however, was unsuccessful and there was leakage from the duct for two weeks, during which the patient lost 13 pounds in weight. The leakage was then controlled by packing with absorbent cotton and the patient rapidly recovered. In the second case the duct was cut directly across, being adherent to involved glands. It was about 3 mm. in diameter and its suture was difficult. The distal end could be seen to dilate with respiration and to eject chyle. The proximal end was collapsed. The posterior portion was held in position by connective tissue surrounding the duct. We were able to do an end-to-end suture by means of very fine curved needles threaded with silk fibre. On completion of the suture, the duct on both sides of it could be seen to distend with respiration and there was evidently free circulation within it. The suture held and there was no leakage after operation, although the wound suppurated, the patient having previously had a streptococcus infection of a sinus. This is the first case of end-to-end suture of the thoracic duct we find recorded. In the third case the duct was nicked and a lateral ligature applied. There was no leakage afterwards. In the fourth case, in separating some very adherent glands in the lower angle of the left side of the neck, the duct was so torn that its ends could not be brought together. It was ligated and no ill effects resulted. It would seem from these cases that leakage from the duct after operation is the thing to be avoided and if possible an immediate suture done.

Allen and Briggs recently report 17 cases of traumatic injury of the thoracic duct in the neck, including those reported by Cushing and others, and suggest that as a preventive measure the patient should be given a quantity of cream a few hours before operation, thus enabling one to more readily recognize the thoracic duct. As to treatment, they recommend packing rather than ligation as offering the best chances for the establishment of collateral circulation. In a very difficult operation for Hodgkin's disease recently done by Dr. Halsted, the duct was cut across close to its entrance into the vein in such a way that the cut ends were separated by a distance of a centimetre, and it was impossible to bring them together. The central end could be seen standing wide open and empty. The duct was ligated both centrally and distally. The patient recovered and showed no bad results.

The *paralyses* resulting from the operation are usually slight. In cases where the parotid lymphatics are involved, a careful dissection must be made to avoid injuring the facial nerve. Occasionally one of the lower branches of this nerve is injured and a slight paralysis of the lower lip results.

This has always proved temporary. There has been temporary injury of the hypoglossal nerve in one or two cases. Paralysis of the sternomastoid and trapezius muscles produces a deformity which is visible. As a rule, patients do not notice it, although, of course, it is to be avoided when possible. There may be slight drooping of the shoulder from paralysis of the trapezius and a sinking in of the neck from atrophy of the sternomastoid. The omohyoid often regains its function after suture, its nerve supply, the descendens noni, being commonly uninjured. The functions of the sternomastoid are assumed by the deeper muscles of the neck, and in no case has there been observed any limitation of motion due to its atrophy or even its complete removal. In a case of carcinoma of the cervical glands we once removed both sternomastoid muscles and there was little if any resulting limitation of motion. The sensory disturbances vary a great deal. In some cases there is practically no loss of sensation in the skin after a short time. In others there is a wide area extending over part of the ear, the neck, shoulder and arm, over which there are marked changes in sensation to touch, temperature and pain but these changes are usually unnoticed by the patient until his attention is called to them. It seems possible that by exposing the cervical plexus as it emerges behind the sternomastoid muscle and cocaineizing it that the whole operation might be done with cocaine anesthesia but this has never been attempted. Occasionally patients speak of a feeling of numbness to which they soon become accustomed. Rarely there are small areas of hyperæsthesia in the skin of the neck. The incisions as a rule heal per primam, although in cases where there has been sinus formation with secondary infection, suppuration may take place.

*Late Results.*—In considering the late results of the operation, a much smaller number of cases can be considered. Fifty-three cases have been absolutely lost sight of, while 22 have not responded to letters; 10 occurring in the last year are much too recent to consider, leaving 58 for examination. Of these, 45 or 77.6% are well with no local or other recurrence, and with negative lungs after periods ranging from 1 to 13 years.

Years...	1	2	3	4	5	6	7	8	9	10	11	12	13
Cases...	6	11	3	3	2	2	6	4	4	0	12	2	1

Of these cases, 24 had had more or less incomplete excision of the glands, 3 had been treated by simple incision and curettement, and 18 by complete excision. It is therefore shown that many cases undoubtedly recover without complete excision, although it is evident, from a consideration of the recurrent cases, that recurrences are much more common after incomplete removal of the glands. The small number of well cases that have had the radical operation is due to the fact that the extensive operation has been a gradual development from simpler measures and was not used in the earlier cases. Of 328 cases reported by Jordan and Bloss, 140 were followed; 73% of all these were well. Eighty-two cases were observed after six years and of these 52.4% were well with no recurrence; 30% had local recur-

rences. Eleven statistics, comprising in all 745 cases, show 54% well, 28% with recurrence, and 18% dead. Our results thus compare very favorably with statistics elsewhere, showing 77.6% well, 15.5% dead, and 6.9% living with recurrence. In 21 cases (15%) of the 143 there have been recurrences. In 2 of these the recurrence was on the opposite side. In 2 it was evident at the operation that the removal was not complete and the recurrence dates from the operation. In 4 cases after complete operation there was recurrence at the seat of operation. All other recurrences followed incomplete removal of the glands, or simple incision and curettement. All of the recurrences were within a year; the average time of recurrence being about four months. Many of the recurrent cases were subsequently operated upon. Of the ultimate results, 5 were lost, 2 were not heard from, 1 is dead of general tuberculosis, 1 developed tuberculosis of the lungs fourteen months later and was subsequently lost, 4 are living with recurrences, and 8 are well. Therefore, about 38% of those cases which recurred after a first operation, complete or incomplete, have remained well after subsequent operations. As previously stated, the condition of the lungs before operation was noted as suspicious of tuberculous involvement in 13 cases and as definitely tuberculous in 7 cases. In Jordan's cases 26% showed involvement of the lung before operation. Of the 13 suspicious cases, 6 have been lost track of, while 2 have not responded to letters. Of the remaining 5 cases, 2 are well with negative lungs and 3 are dead, one of tuberculous peritonitis two years after operation, the other 2 from causes not tuberculous, 4 years after operation. Of the 7 showing positive evidence of tuberculosis of the lungs, 2 are lost, one is well two years after operation, one has general tuberculosis, while 2 have died with tuberculosis of the lungs, and one with general tuberculosis. Only one case with definite tuberculosis of the lungs before operation is, therefore, known to have recovered. There are records of 3 cases in which operation was not advised and the patients were not treated because of tuberculosis of the lungs. The experience of Jordan is much more encouraging. Of 140 cases, 20 had lung involvement before operation. At a later examination 16 of these were well and also free from glandular disease, and he concludes that the removal of the glands has a distinct curative effect in 80% of the cases. On the other hand, only one of our cases is known to have developed tuberculosis of the lungs after operation where the lungs were negative before operation, while 13 of 140 of Jordan's cases developed lung complications after operation. Unfortunately, our one case has been lost, the only note on the history being that the patient presented himself 14 months after operation with tuberculosis of the lungs. There have been 9 deaths in the 58 cases followed (15.5%). Two of these died of heart disease, one four years, one six years after operation; one of an acute non-tuberculous illness one year after operation; one from unknown cause 4 years after operation; one of tuberculosis of the lungs a year after operation; one of tuberculous peritonitis two years after operation, and three with

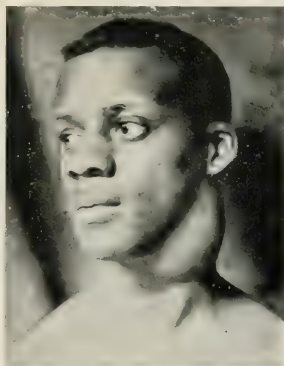


FIG. 1.—Characteristic tumor formed by tuberculous glands of neck.



FIG. 2.—Hodgkin's Disease forming large tumor in neck.



FIG. 3.—Keloidal scar and area of anæsthesia following complete excision of glands of neck.



FIG. 4.—Extensive anæsthesia following complete excision of glands of left side of neck.

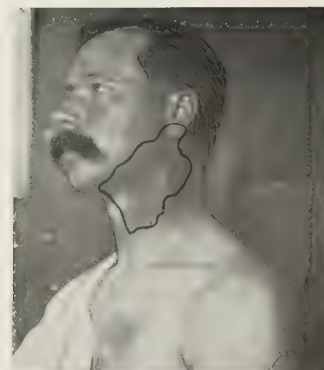


FIG. 5.—Small area of anæsthesia where attention was paid to saving branches of cervical plexus in recent operation.





FIG. 6.—Marked droop of shoulder due to division of posterior branch of spinal accessory nerve. Area of anesthesia following complete excision of glands of right side of neck.



FIG. 7.—Area of anesthesia 2 years after excision of glands of neck with removal of sternomastoid and omohyoid muscles, internal jugular vein and common carotid artery.

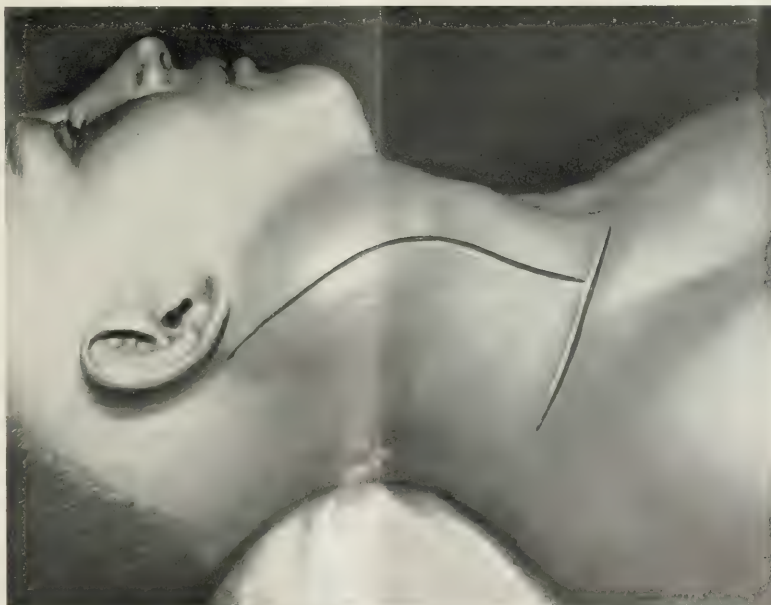


FIG. 8.—Skin incision for complete removal of glands of neck.



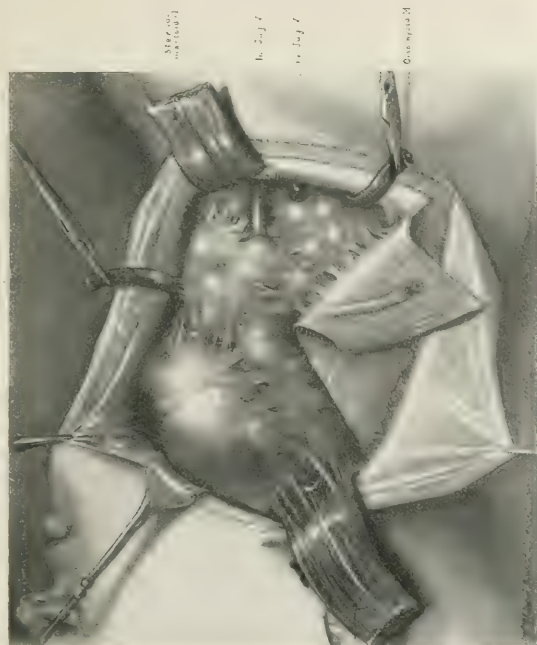


FIG. 10.—Omohyoid and sternomastoid muscles divided and reflected; external jugular vein ligated and divided.



FIG. 9.—Skin flaps reflected showing quadrilateral exposure of all parts of the neck obtained through the T-shaped skin incision.

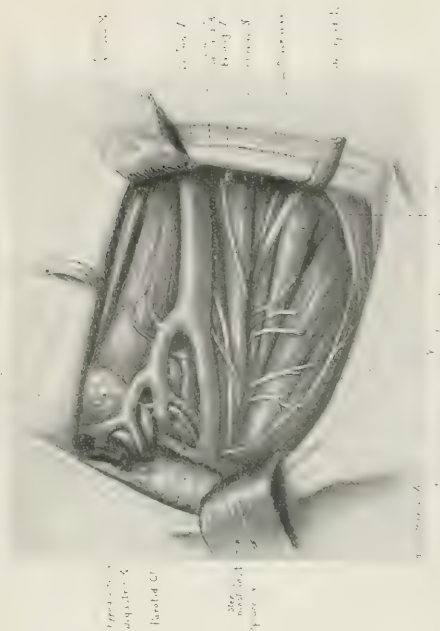


FIG. 12.—After complete removal of glands. Spinal accessory nerve intact, its posterior branch given off before entering sternomastoid muscle showing its anastomosis with cervical plexus.



FIG. 11.—Glands dissected away from internal jugular vein.



general tuberculosis. Thus five cases have died of tuberculosis after operation. In the cases of Blos and Jordan there were 19% of deaths in 12 years. Eighteen of these were from tuberculosis. These statistics would indicate a much closer relation between tuberculosis of the glands of the neck and tuberculosis of the lungs than our cases show, and it is stated that about 28% of all usually die of tuberculosis elsewhere after operation. This corresponds very closely to the results in tuberculosis of the knee where it is stated that from 20% to 30% of all cases prove fatal from tuberculous affections. Unless there is general dissemination of the disease tuberculosis in other regions than the lungs is extremely rare after operation. One of our cases developed tuberculosis of both thumbs and is now well after subsequent operations. One had Pott's disease and later died of general tuberculosis, and one died of what was, from the physician's description, apparently tuberculous peritonitis.

*Conclusions.*—From the study of our own cases and their subsequent observation, and from the results of others, the following conclusions can be readily drawn:

(1) Tuberculous cervical adenitis is primarily a local disease of very frequent occurrence, more often in young persons; in itself not extremely serious and rarely if ever proving fatal.

(2) It bears, however, a certain definite relation to tuberculosis of the lungs and serves as the starting point from which tuberculosis may spread.

(3) The tuberculin test as an aid to diagnosis is positive and harmless.

(4) While recovery may often take place under good hygienic conditions, surgical interference is clearly demanded in most cases.

(5) When surgical treatment is resorted to the operation should be radical in all cases.

(6) Recovery may be predicted in 70-80% of cases so treated. Tuberculosis of the lungs after complete removal of the glands is comparatively rare.

(7) Tuberculosis of the lungs unless far advanced is not a contraindication to operation, the removal of the glands apparently exerting a beneficial influence on the condition of the lungs.

#### LITERATURE.

No attempt has been made to review all the literature. Extensive bibliographies will be found under references 1, 2 and 3.

(1) Blos, Edwin: *Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie*, 1899, IV, p. 520.

(2) Jordan: *Handbuch der praktischen Chirurgie*. Bergmann, Bruns und Mikulicz, 1900, II, p. 84.

(3) Dowd, Charles N.: *Annals of Surgery*, 1899, XXIX, p. 559.

(4) Cheyne, W. Watson: *British Medical Journal*, 1899, No. 2033, p. 1659.

(5) Harnett, C. J.: *Guy's Hospital Reports*, 1901, Vol. LV, p. 55.

(6) Allen, Dudley P., and Briggs, C. E.: *American Medicine*, September 14 and 21, 1901.

## THE LEUCOCYTE COUNT IN THE SUMMER DIARRHOEAS OF CHILDREN.<sup>1</sup>

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Perhaps no subject in medicine has been more thoroughly worked over during the last few years than that of the blood. The chemical constituents of this fluid have been subjected to as searching analysis as the present state of chemical knowledge will permit, and to the data thus obtained very much of great importance has been added in the physiological and pathological laboratories. The several proteid bodies in the blood have been studied and their relationship to the gases and mineral solids in large part determined. More accurate methods have been introduced to estimate other principals which are present in normal blood in small quantities but which are of pathological significance when in excess. Among these substances may be mentioned urea, uric acid, glucose, glycogen, ferments, fat and bile. More interest of late years has been given to acetone and diacetic

acid which have been shown to be poisonous and the cause of diabetic coma. Careful work has been done also on the specific gravity of the blood, in the determination of its exact alkalinity and its osmotic tension.

In recent years the newly discovered properties of blood serum in connection with the production of immunity and its agglutinative action on specific bacteria, infecting the normal body, have given to the blood a prominence in diagnosis and therapy which is shared by no other tissue.

That many more untrodden paths are just ahead in this field of investigation, the work of Ehrlich and others leads us confidently to anticipate.

Much of the recent work just suggested has been possible only in laboratories equipped with expensive apparatus and has required for its performance considerable special knowledge not possessed by the practicing physician. It is rather to the study of the *formed* elements of the blood, to the con-

<sup>1</sup> Paper read at the 104th Annual Meeting of the Medical and Chirurgical Faculty of Maryland, April 24, 1902.

sideration of the number, size and appearance of the red and white cells that he has devoted most attention. Naturally the path has been pointed out step by step by laboratory men, who as skirmishers have blazed the way through the wilderness, in suggesting new stains and better methods to the great army of practitioners following after, and eager for more light in their conflict against disease. In this way a blood examination, at least to the extent of a microscopic survey of a specimen of fresh blood, has become almost as customary in hospital and private practice as the use of the stethoscope or the examination of urine.

The story of the great diagnostic help of even this hasty method need not be here repeated. The medical journals have for several years been eloquent witnesses to the value of a blood examination in many of the maladies common in both medicine and surgery. By means of the fresh preparation referred to, almost invaluable information can be obtained as to the size and color index of the red corpuscles, the relative number of white cells can be roughly estimated with a little practice, and the presence or absence of blood diseases, as anæmia or leukæmia, can be determined. Of more importance still, such an examination should enable one to detect the malarial parasite, if present, and so relieve this interesting plasmodium from the odium of producing every disease which baffles the diagnostic acumen of the doctor.

It is in relation to affections other than that of the blood itself, that the enumeration of the white cells together with a differential count as to the exact percentage of each variety of cell, is of more general diagnostic importance. That the leucocytes are reduced in number in typhoid fever, malaria, miliary tuberculosis and several other affections and increased in pneumonia, bronchitis, appendicitis and other inflammatory processes, is now well known. Although information obtained through this blood count must be weighed in the balance with that from other sources, a knowledge of the number and variety of the white cells and the rapidity of their increase or decrease when rightly interpreted, often affords most valuable information concerning the condition of the patient.

It is rather strange that while the counting of the leucocytes has been employed for years in the practice of medicine among adults, similar methods are not so generally in vogue in pediatrics. This is the more remarkable because in this field of medicine the physician cannot obtain information from the patient concerning the exact subjective symptoms, but must depend almost entirely upon objective signs and the result of his own examination. *A priori* one would think that a knowledge of the blood condition of his patient would be sought early by the pediatrician in the examination of his case, though there are several important differences between the normal condition of the blood in early, as compared with that in later life, which must be appreciated before the examination of the blood of children can be made of much value. It has long been known that the

number of red corpuscles is considerably larger in the new born than in the adult; the average of several investigators, including Hayem, Otto, Gundobin and Elder and Hutchison and others quoted by Stengel and White<sup>2</sup> is 5,740,080 per cmm. After a few days, according to Schwinge and Gundobin,<sup>3</sup> this number gradually decreases throughout the first year, after which there is an increase up to the eighth or twelfth year when the number becomes that maintained until adult life. Greater irregularities in the size of the red cells during the first stage of life are described by Hayem, Loos and Gundobin. Many writers<sup>4</sup> have called attention to the increased hæmoglobin content and rather high specific gravity of the blood of infants.

The leucocyte count interests us particularly; it ranges at birth from 14,000 to 27,000 cells to the cubic millimeter. There is a decrease during the third and fourth days, after which time for the first year of life a general mean of 10,000 to 15,000 leucocytes per cubic millimeter is maintained.

Hayem states that the count at fifteen months is about 10,000 cells. Head<sup>5</sup> affirms that after the second year in healthy children the number of leucocytes is about that in adult life and that a leucocytosis in a child over two years of age has the same significance as in an adult.

Another interesting difference in the white cells in childhood is their altered differential count. This varies greatly, as reported by several investigators, and the results are rendered somewhat uncertain by the adoption of several systems of classification. Using Ehrlich's well known scheme, Gundobin<sup>6</sup> and other recent writers give the following as normal in infancy:

Lymphocytes .....	50-66%
Polymorphonuclears .....	28-40

Ehrlich's figures may be taken as standard for an adult; they are:

Lymphocytes .....	22-25%
Large mononuclear and transitional forms..	2-4
Polymorphonuclears .....	70-72
Eosinophile cells .....	2-4

Thus one sees that in childhood the proportion of lymphocytes is usually much increased and that of the polymorphonuclear cells correspondingly diminished. The number of eosinophiles reported by different writers is so various that further investigation is necessary to establish a mean for early childhood.

As one would anticipate, the blood of infants is in a state of less stable equilibrium than that of adult life. The organism is nearer its embryonic period and the blood-forming centers in the bone marrow and lymph glands are in a

<sup>2</sup> University of Penn., Med. Bull., Vol 14, 1901, p. 310.

<sup>3</sup> Loc. cit. p. 312.

<sup>4</sup> A. Monti, Das Blut und seiner Erkrankungen. Pages 572 and 582.

<sup>5</sup> Arch. of Ped. Vol. 19, 1902, p. 254.

<sup>6</sup> Jahrbuch f. Kinderheilk. vol. xxxv, 1893.

state more responsive to stimulation than in later years. Thus the well known digestive leucocytosis is more marked in infancy than at any other time; an increase of 2000 to 4000 leucocytes has been noted after the ingestion of food. So too there is a quicker response after hæmorrhage, and anæmias of only moderate grade are associated with nucleated red cells and myelocytes in the circulating blood. This and similar factors must be reckoned with in attempting to form an idea of any changed condition in the blood of an infant in the course of a disease. Such difficulties should spur one on to greater efforts to place more counts on record and as the tables grow, it is to be hoped that a number of deductions, helpful in the diagnosis of many of the maladies common in infancy may be possible.

Of all the diseases of infancy none is more deadly in its results nor has so defied the medical profession in their efforts to determine its etiology and proper treatment than the group of closely allied ailments classed together as the "summer diarrhæas." The mortality in our large cities from this cause is hardly appreciated by the physician or layman. Thus in Baltimore in the year 1901 the total mortality of children under five years was 2552, of this number the deaths from intestinal diseases was 732, that is nearly 30 per cent of the total death rate among children was due to diarrhæal diseases. It is particularly fitting therefore to study summer diarrhæa from every possible standpoint and the consideration of the leucocytes, although developing no new or startling facts, will at least have a negative value. It is surprising how few reliable observations there are upon this important subject. Guffer<sup>7</sup> in 1876 found that in chronic atrophy there was a decrease in the number of red cells and an increase in the number of leucocytes. Parrot later made a similar observation. Fischl<sup>8</sup> in a valuable contribution on the study of blood in infants asserts that inflammation of the intestinal tract is accompanied by leucocytosis and that the lymphoid cells are particularly increased. A year later Weiss<sup>9</sup> reported a leucocytosis in eight cases with a similar increase in the small round cells which he thought to be due to a stimulation of the lymphoid apparatus of the intestine. These results, although probably erroneous, have been transferred to several text-books on the blood.<sup>10</sup> In the same year Gundobin<sup>11</sup> reported twelve cases of gastrointestinal catarrh in children in which he found a leucocytosis and an increase in the over-ripe elements, the form in Uskoff's scheme corresponding to the polymorphonuclear cells in Ehrlich's classification of leucocytes.

A later series of twenty cases is reported by d'Olandi<sup>12</sup> in 1899. Most of his patients suffered from chronic forms of enteritis, secondary often to rickets. He observes usually

a moderate leucocytosis and a differential count showed an increase in forms which correspond to the polymorphonuclear variety in Ehrlich's classification.

The most complete study of the leucocytes in diseases of the digestive tract in infants appeared in April of last year by Alfred Japha<sup>13</sup> from Heubner's clinic in Berlin. In order to establish a standard for comparison Japha counted the leucocytes many times in a series of twenty-two children under one year of age who were well or suffering from mild illnesses not of the intestinal tract. He found on taking the average of his count the following results:

Leucocytes .....13,560

Differential count:

Lymphocytes .....54%  
Large mononuclear cells ..... 4  
Polymorphonuclear cells .....42

His results showed considerable variations, but that age, weight and temperature within limits, made no difference. The increased leucocytosis in childhood, he points out, is due to the large percentage of lymphocytic cells.

He then began a series of counts of the leucocytes in the blood of children who were suffering at the time of investigation from dyspepsia or colic; these showed no marked change from his established standards either in the number of leucocytes or in their differentiation into groups. Another series of children suffering from chronic dyspepsia or atrophy presented a similar leucocytic picture. He then divided the cases remaining into three groups:

1. Gastrointestinal catarrh—characterized by foul mucous stools and fever.

2. Follicular enteritis. The cases were many of them fatal. There was rapid wasting with or without fever. The stools contained mucus and blood and often streptococci were demonstrated.

3. Cholera infantum. These cases showed all the symptoms of acute intoxication. Nearly all of them ended fatally.

The leucocyte count in series 1, gastrointestinal catarrh—showed leucocytes varying from 10,300 to 36,000. On differential count an increase in the percentage of the polymorphonuclear leucocytes was demonstrated. They varied in this group from 47% to 55%, while the lymphocytes were reduced to from 38% to 51%.

In group 2, follicular enteritis, this increase in the percentage of polymorphonuclear cells was also noticed. The total number of leucocytes varied within wide limits, depending apparently upon the activity of the body in resisting infection and upon the concentration of the blood. Thus in one case there were but 15,000 white cells while in another there were 38,000. The percentage of polymorphonuclear cells varied from 40% to 75%, average about 60%, and that of the lymphocytes from 18% to 50%, average about 35%.

<sup>7</sup> Revue mensuelle 1876. Cited by Fischl.

<sup>8</sup> Zeitschr. f. Heilkund. 1892.

<sup>9</sup> Jahrbuch f. Kinderheilk. vol. xxxv, 1893.

<sup>10</sup> Ewing, Clinical Pathology of the Blood, p. 344.

<sup>11</sup> Loc. cit.

<sup>12</sup> Rev. Mens d. mal. de l'enf., Joullet, 1899.

<sup>13</sup> Jahrbuch f. Kinderheilk., vol. liiii, 1901. p. 179.

## GROUP A.—DYSPEPSIA.

Name.	Age.	Duration of disease.*	Leucocytes.	Polymorpho-nuclears.	Small mononuclears.	Large mononuclears transitional.	Eosinophiles.	Myelocytes.	Character of stools.	Results.	Remarks.
Annie Ehm, I.....	6 mos.	5 days	13,900	37.8%	39.7	21.2%	2.5%	.0%	Fluid, some mucus.	Well.	Onset with numerous loose stools, vomiting. Mild case.
Bertha Amend, II....	14 mos.	6 days	36,500	39.2	41.8	18.6	.4	.0	Semi-fluid, no mucus.	Well.	Onset with vomiting and offensive stools. No blood.
Margaret Pierce, III..	4 mos.	16 days	13,500	19.8	64.	14.6	1.	.8	Fluid, no mucus, no curds.	Well.	Onset 2 weeks before with loose bowels, some fever. Child admitted late in disease.

## GROUP B.—DYSPEPTIC DIARRHÆA.

Katherine Moore, I...	2 yrs.	10 days	24,000	66.2	17.	13.4	2.8	.4	Pasty, yellow, casein and blood.	Well.	Mild case, child about convalescent.
Leslie Keller, II.....	5 mos.	....	....	39.8	38.2	20.2	1.2	.6	Yellowish green, mucus.	Improved.	Irregular bowels since birth. No vomiting or fever.
Elmer Buenger, III...	14 mos.	24 days	7,000	50.2	20.2	28.6	1.	.0	Watery, greenish mucus.	Improved.	Readmitted with history of blood in stools and irregular bowels for three weeks.
Adeline Turk, IV....	20 mos.	11 days	21,000	63.2	26.6	8.8	.4	1.	Dark, semi-fluid, no lumps.	Improved.	Frequent watery stools, great prostration, blood once.
Estella Wise, V.....	13 mos.	....	....	41.2	37.2	16.6	3.4	.0	Curds, no mucus.	Well.	Very severe case. High fever. Sharp attack, no blood in stools, child seen late in disease.

## GROUP C.—ILEO-COLITIS.

Lydia Seehagen, I....	9 mos.	5 days	16,300	63.8	9.6	26.2	.4	.0	Yellowish green, mucus.	Improved.	Child in poor condition when admitted. Very ill while in hospital.
Marion Sykes, II.....	7 mos.	14 days	11,500	63.	23.	10.6	2.8	.6	Curds, mucus, some blood.	Unimproved.	Sudden onset, blood in stools, no vomiting, no fever.
Charles Powell, III...	6 mos.	5 wks.	27,600	78.	9.6	10.6	.0	1.8	Fluid, light green.	Died.	History of blood in stools. Onset 2 weeks. Emaciated child. In hospital 3 weeks, unable to retain food.
Barrett Baum, IV....	7 mos.	6 days	41,000	78.4	14.6	6.4	.6	.0	Mucus, traces of blood.	Died.	Malnutrition. Autopsy. Marked prostration.
Bennie Ambrose, V...	1½ yrs.	13 days	58,000	72.4	19.6	5.	1.2	1 normoblast	Fluid, mucus and pus.	Unimproved.	Ulcerative colitis found at autopsy.
Charles Graves, VI....	1 yr.	14 days	14,000	56.3	33.6	10.	.0	.0	Blood and mucus.	Died.	Onset with mucus and blood in stools.
Charlie Zelinka, VII..	4 mos.	12das.(?)	27,000	75.2	14.2	10.6	.0	.0	Fluid, no mucus, no curds.	Died.	Autopsy showed ulceration of colon.
Alice Constandt, VIII	1 yr.	4 wks.	33,300	59.4	24.4	15.3	.3	.0	Mucus, no blood.	Died.	Vomiting, blood in stools. Autopsy showed ulceration of colon.
Hammond Rice, IX...	2 yrs.	6 wks.	14,100	51.4	31.2	17.	.4	.0	Semi-fluid, mucus.	Well.	Autopsy showed ulceration of lower descending colon.
Isadour Rosenthal, X 2½ yrs.	6 days	....	76.6	7.	15.	1.4	.0	.0	Blood and mucus.	Improved.	Onset with mucus and blood in stools, marked emaciation.

## GROUP D.—CHOLERA INFANTUM.

Margaret Ritter, I....	11 mos.	2 days	...	76.4	13.4	9.8	.4	.0	Fluid, blood.	Died.	Treated for 1 mo. for dyspeptic diarrhœa. Suddenly developed symptoms of intense toxemia. Rickets.
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## GROUP E.—INFANTILE ATROPHY.

Name.	Age.	Duration of disease.	Leucocytes.	Polymorphonuclears.	Small mononuclears.	Large mononuclears and transitionals.	Eosinophiles.	Myelocytes.	Character of stools.	Results.	Remarks.
Thomas Johnson, I..	4 mos.	25 days	20,000	40.6	45.6	12.4	1.4	.0	Small homogeneous. Occasional trace of mucus.	Died.	Child suddenly removed from breast because of illness of mother.
Margaret Herold, II..	3 mos.	40 days	13,600	45.4	31.8	20.4	.8	1.4	Dark green, semi-fluid. Occasionally mucus.	Died.	Child lost weight from age of 2 mos. condensed milk feeding. Rickets.
Helen Taylor, III....	3 mos.	42 days	18,600	52.2	38.2	8.4	.2	1.	Semi-fluid, greenish, trace of mucus.	Improved.	

## GROUP F.—INFANTILE ATROPHY COMPLICATED.

Mary Blackwood, I...	7 mos.	40-45 days	13,000	74.8	17.8	.7	.2	1.2 10 normoblasts.	Large, viscid, fairly homogeneous.	Died.	Colitis found at autopsy. Stools just before death contained blood.
Lilian Davies, II....	5 mos.	....	....	67.8	20.	9.4	.6	2.2	Fluid, greenish, some mucus.	Died.	Steady loss in weight from onset. Peculiar dark bronzing of skin. No autopsy.
Jane Viszkinskao, III..	4 mos.	60 days	24,000	69.4	15.	14.2	.4	1.	Yellowish green, semi-fluid. Fairly homogeneous.	Died.	Steady loss in weight. Autopsy showed mild colitis. No extensive ulceration.

\* By "Duration of Disease" is meant from time of onset to time when blood was taken.

In the last group, 3, comprising the cholera infantum cases, the leucocytosis was more constant, the white blood corpuscles varying from 51,000 to 54,000 per cubic millimeter. The polymorphonuclear cells averaged about 65% and the lymphocytes about 25%, although there were marked differences in the individual cases.

These results correspond so closely to a series of counts made by one of us last summer at The Thomas Wilson Sanitarium that we venture to incorporate them in the nature of a preliminary report, as it is hoped that a more complete investigation can be conducted during the coming season. Our cases, twenty-four in number, are briefly summarized in the accompanying table.

The blood was collected in the usual manner on cover-slips and fixed by heating over a copper bar or in absolute alcohol and ether, and then stained by Ehrlich's triple stain. A number of the specimens were air dried and stained with Jenner's stain, which gave excellent results. At the time of obtaining the blood for the specimens the leucocyte count was made. All our patients suffered from some form of digestive disturbance; most of them were extremely ill and were seen rather late in the course of disease.

They can be arranged according to their symptoms into groups corresponding with those of Japha, although the several grades of the affection merge, the one into the other, and the division line must be to some extent artificial.

The blood of several well babies was counted for comparison; it averaged about as follows:

Polymorphonuclears .....	35%
Small mononuclears .....	50
Large mononuclears .....	11
Transitionals .....	3
Eosinophiles .....	1

Three cases were counted which belonged to group A, in which the disturbances were of mild grade; they resulted thus: The leucocytes varied from 13,500 to 36,000.

Differential count was as follows:

Polymorphonuclears .....	37.8%
Small mononuclears .....	39
Large mononuclears .....	19.2
Transitionals .....	2
Eosinophiles .....	2

In this group the normal differential count was but slightly altered.

Group B. Dyspeptic fomenta diarrhoea; here the leucocytosis was of mild grade, about 21,000. The analysis of the count shows an increase of the polymorphonuclear forms as follows:

Polymorphonuclear leucocytes .....	39	to 63%
Large mononuclear leucocytes .....	8	to 26
Transitionals .....	.4	to 2
Eosinophiles .....	.4	to 3.4

The next group, the largest, group C, comprises those cases where symptoms or autopsy revealed marked inflammatory changes in the intestinal wall. The leucocytes varied from 16,000 to 58,000.

Polymorphonuclear leucocytes .....	56-78%
Small mononuclear leucocytes.....	7-33
Large mononuclear leucocytes .....	3-21
Transitionals .....	0- .4
Eosinophiles .....	0- 1.4

Group D. A case which showed symptoms of acute intoxication and should be classed as cholera infantum and had practically an identical blood count.

In group E are gathered those cases of infantile atrophy without many symptoms of digestive disturbances. Here the leucocyte count varied from 13,600 to 20,000, distributed as follows:

Polymorphonuclear leucocytes .....	40-52%
Small mononuclear leucocytes .....	31-45.6
Large mononuclear leucocytes .....	3-18
Transitionals .....	0- 2.7
Eosinophiles .....	2- 1.4

Group F included those cases of atrophy or marasmus in which usually as a terminal infection there is in addition, inflammation of the intestine. In these cases there was little increase in the leucocyte count which varied from 13,000 to 24,000. The differential count was as follows:

Polymorphonuclear leucocytes .....	57-74%
Small mononuclear leucocytes.....	15-20
Large mononuclear leucocytes .....	6-13
Transitionals .....	4- .8
Eosinophiles .....	2- .6

In every case but two, 500 leucocytes were counted.

It will be noticed that the count obtained in a number of the cases, e. g., group A all cases, group B cases 2 and 3, group C case 1, group E case 2, showed a large percentage of large mononuclear cells. This apparent increase may be explained by the following facts. In infants' blood the different forms of leucocytes are not so sharply defined as in the blood of adults, and so there are constantly seen cells of a mononuclear variety which are neither lymphocytes nor typical large mononuclear leucocytes, and the group in which the somewhat doubtful cell is placed must be determined by the personal equation of the counter. All mononuclear cells larger than the average sized polymorphonuclear leucocyte were called by us large mononuclear cells. It is to be noted, as seen in the table, that the cases of the highest percentage of the large mononuclear cells as a rule did well, whereas in those cases in which the percentage of these cells was low either died or were unimproved. However a much larger series of cases must be taken before anything conclusive as to the prognosis can be drawn from these findings. Myelocytes were found in only a few of the cases and the percentage was never high. No importance can be attached to their presence in our series. In only two cases were nucleated red blood cells seen and these were

normoblasts (group C, case V; group F, case I). In a number of cases no eosinophile cells were seen in counting 500 leucocytes. This tallies with the observations made by several observers tending to show that these cells, as far as known, have little significance in these disorders.

A comparison of our findings with those of Japha indicate that leucocytosis in cases of this nature is no index of the severity of the attack.

As pointed out by Rieder,<sup>14</sup> the following varieties of leucocytosis produced by pathological influences may be distinguished.

1. Inflammatory.
2. Toxic.
3. Post hæmorrhagic.
4. Cachectic.
5. Agonal or premortal.

In summer diarrhœa the leucocytes are similarly increased in the ulcerated inflammation of the intestine and in acute autointoxication, and their simple enumeration affords little aid to diagnosis. Their number is also affected by other factors, such as the specific gravity of the blood, the resistance of the patient, etc., which factors are not as yet thoroughly understood.

Of more moment than the number of the white cells is their differential count. The results enumerated above would seem to indicate that the more severe the infection the greater the number of polymorphonuclear leucocytes in relation to the mononuclear forms.

Our conclusions may be briefly summarized as follows:

1. A differential count of leucocytes in the blood of well children under two years of age, when compared with the blood of adults, shows that there is a relative increase in the small mononuclear elements and a decrease in the number of polymorphonuclear cells.

2. In the summer diarrhœas of infants the number of leucocytes in the blood is usually increased but the count of the white cells varies within such wide limits, even in the milder forms of the affection, that a high or low leucocytosis cannot be regarded as of diagnostic value.

3. In the simple dyspepsias of childhood a differential count of the leucocytes does not show any marked variation from that of a healthy infant, but as the cases become more severe in type there is apparently a progressive increase in the polymorphonuclear neutrophile cells and a decrease in those of the small mononuclear variety, thus presenting a picture more like that of adult blood.

4. As pointed out by Japha, the polymorphonuclear leucocytosis is an indication of an intoxication with decomposition products in the intestine or of the toxins of pathological bacteria; i. e., it takes place both in the cases of acute intestinal poisoning and in the more severe forms of ileocolitis.

5. The cases of simple infantile atrophy present a nearly normal differential leucocyte count, but it would seem that an increase of the polymorphonuclear cells may indicate the setting in of an inflammatory intestinal complication.

<sup>14</sup> Quoted by Monti, Loc. cit., p. 594.

## TYPHOID FEVER: REPORT OF A CASE WITH THREE RELAPSES. REMARKS.

BY LOUIS M. WARFIELD, M. D.,

*House Medical Officer, The Johns Hopkins Hospital.*

*CASE.*—*Typhoid fever of long duration. Severe initial attack, hemorrhages; three relapses and three recrudescences; recovery.*

L. D., white, female *æt.* 12, Hosp. No. 35,764, was admitted August 5, 1901, to the Johns Hopkins Hospital in the service of Dr. Osler, on the 4th day of disease, complaining of pain in the stomach, headache and fever. Beyond a history of consumption in the family, the family history is unimportant. She herself had previously been fairly strong and healthy. She had had none of the acute infectious diseases except measles and whooping cough. There was a history of chills and fever, 14 months ago, lasting about one week. Menstruation has not yet been established. For two months past she has had no appetite, has felt tired out and has complained continually of headache and backache. Since June she has had a dry hacking cough without expectoration and her cheeks have been constantly flushed. She had no night sweats, chills, or epistaxis. Since August 2 she has been in bed with high fever. For several days before her admission she complained of pain in the abdomen and the night before admission she was delirious. She had lost considerable flesh and strength during the past two months. She drank unboiled hydrant water. No one else in the house was ill.

*Condition on Admission.*—Fairly well nourished child. Examination of lungs and heart showed nothing abnormal. Pulse 92 to the minute, not dicrotic, regular. Abdomen not distended, respiratory movements free throughout. No rose spots. Spleen just palpable when she lies on her right side. No abdominal tenderness. Hepatic flatness just reaches the costal margin in the right mammary line. No delirium.

There was some diarrhœa on admission, the stools being "pea-soup" in consistency, but her bowels soon became fairly regular and remained so throughout the whole illness. The urine showed a marked diazo-reaction. There were no albumin and casts. The examination of a fresh blood smear showed no malarial parasites but a curious vacuolic degeneration of the leucocytes was noted. The count per cmm. was: erythrocytes 4,956,000, leucocytes 12,600, hemoglobin 82 per cent. From blood cultures taken on August 6 a pure culture of *B. typhosus* was obtained. On August 7 rose spots were found over the abdomen. On August 8 the Gruber-Widal reaction was positive in dilution of 1:50.

The patient was given ice sponges for three days, then put in a tub bath at 85° every three hours whenever her temperature reached 102.5° or over. She did very well up to August 15; at 9 a. m., when she had a hemorrhage of bright blood, about 150 cc., followed by a continuous bleed-

ing, amounting in all to 500 cc. She became slightly collapsed. Her pulse became imperceptible after the last hemorrhage. There was some pain in the abdomen. That night she had two more hemorrhages, losing in all about 760 cc. of blood. She was infused with normal salt solution and given a 2 per cent solution of gelatin subcutaneously. In addition she had morphia and lead and opium. She was infused again at night as her condition was very grave. An ice bag was kept over her abdomen and all nourishment was ordered to be withheld for 24 hours. The leucocytes, which had been 4000-7000, now rose to 12,000, her red blood corpuscles were 4,484,000, and hemoglobin 78 per cent. She rallied well and her pulse had improved markedly when on August 16, she became very restless and somewhat irrational. The abdomen was tender but not until afternoon of August 16 did she complain of severe abdominal pain. At that time there was exquisite tenderness in the lower quadrant of the abdomen with definite rigidity and muscle spasm, but on closer examination similar tenderness was found over her thigh and it was not long before the muscle spasm and rigidity had completely disappeared. Her condition remained about the same throughout afternoon and night. She had voided urine in the meantime and when seen at 11 p. m. by Dr. Fletcher the note was as follows: "Her features are distinctly drawn at times. The abdomen is not distended. Respiratory movements if anything are slightly less marked than at 6 o'clock. She cries out at times with pain which it is difficult to get her to locate owing to her semidelirious condition. The slightest pressure over the right lumbar and iliac regions causes acute pain and there are definite muscle rigidity and spasm on the right side but none on the left. Liver dullness still reaches the costal margin. It is not possible to test for movable dullness in the flanks. She has not vomited. The pulse volume is not quite so good as it was earlier in the day. It has continued practically 120 since 6 o'clock." Owing to the variability of the pain, the similar pain over the thigh together with the fact that her condition grew no worse, the symptoms were considered to be due to a neurotic condition. A blood count made during the day showed red blood corpuscles 3,292,000, white blood corpuscles 4000, hemoglobin 40 per cent.

August 17. Her condition decidedly better but she is still delirious. Her temperature continued high (see chart). The pulse improved and abdominal tenderness was not nearly so marked. Her leucocytes were 3900 and hemoglobin 40 per cent. She developed a cough during the next few days and a bed sore over sacrum.

On September 2, the thirty-second day of her illness, her

temperature touched normal. From that date until September 27 it was practically normal, showing an occasional rise to 99°. She seemed apparently quite well, and was about to be discharged when suddenly on September 28 her temperature rose to 103.2° and she had headache but no diarrhoea. She looked rather ill; her tongue was slightly coated, her pulse 100 and not dicrotic. The spleen was not palpable and no rose spots were seen on the abdomen. On October 3 rose spots were seen and the spleen was palpable. Blood cultures were taken again and *B. typhosus* was obtained in pure culture. The urine showed considerable albumin and quantities of pus cells and the diazo-reaction which had not been obtained since the primary attack of fever, was again positive. A blood count showed red blood corpuscles 3,988,000, white blood corpuscles 4600 and hemoglobin 58 per cent. Her condition was good; she suffered no pain and on October 3, the sixty-third day of her stay in hospital and sixth day of her relapse, her temperature touched normal. It oscillated slightly above and below normal for four days, during all of which time the spleen was palpable but becoming smaller every day. On October 8 her temperature suddenly rose to 103.7°. On October 12 there was a sharp intercurrent rise and the patient appeared quite ill. Her leucocytes now rose to 12,700 and besides the albumin in the urine, some red cells were seen under the microscope. She complained of slight abdominal pain; spleen readily palpable. Her temperature continued between 101.6° and 104.5° until October 17, when it touched normal again. From October 18 to 20 she was afebrile. Her pulse was slow and of good volume and tension. October 19 her spleen was just palpable. From October 20 to 26 she had another febrile period during which rose spots appeared on the abdomen but the spleen was not palpable. Her temperature was practically normal until October 31, when it rose to 102.5°. Her leucocytes, which had, since the last rise, fallen to 7000, rose to 14,500. There were no rose spots but her spleen again became palpable. November 2, rose spots were seen on abdomen. Her temperature showed marked oscillations to November 4. She then appeared in good condition, was quite bright. There was considerable cyanosis of trunk and limbs although her temperature was normal. On November 7 a few fresh rose spots were seen, the spleen, however, was not palpable. There was an irregular temperature, at times reaching 102.6°, but on November 13, with this temperature and a rapid pulse, there were no fresh spots and her spleen was not felt. On November 18 her temperature became normal and remained so for 11 days. She was again apparently well and almost ready to go home. On November 30, the 121st day of her illness and 64 days since the first relapse, she complained of a headache. Her temperature was 100° at 6 a. m., rising at 2 p. m. to 103.7°. She was listless and apparently felt badly. Her pulse was 140, rather small; spleen readily palpable; no rose spots; abdomen natural, not tender. Her temperature remained elevated for 60 hours when it became normal and she passed

on to complete recovery. She was discharged December 15 after a residence in the hospital of 136 days.

Relapses in typhoid fever are unfortunately common enough and vary greatly in different places and in different years. Multiple relapses, by which we mean three or more relapses, are however not common. Da Costa<sup>1</sup> mentions in a clinical lecture that he has seen two cases with five relapses each, both of whom recovered. Jaccoud and Netter<sup>2</sup> each report a case with five relapses. No cases with more than five relapses could be found in the literature.

Carslaw<sup>3</sup> reports a case with four distinct relapses, lasting from August 10 to March 6, when the patient was discharged well. The initial attack lasted 34 days. The patient was very ill, had hemorrhages from the bowels and was in *extremis*. She survived and her temperature fell by lysis and was normal for two days. It then rose and she had a relapse lasting 23 days. There was an interval of apyrexia of 15 days when the temperature again rose and patient entered on the second relapse. Rose spots were noted for the first time. This relapse lasted 22 days and was followed by normal temperature for 10 days. There was a third elevation lasting 16 days complicated with *plegmiasia alba dolens* of one leg. Again the temperature became normal and remained so for 16 days when she had a fourth relapse lasting 10 days. Recovery was complete.

Béna,<sup>4</sup> in his series of 598 cases in Strassburg from 1872-91 and 168 cases in Königsberg from 1877-87, found 79 single relapses, 13 double relapses, 6 with three relapses and one (partially reported only) with five relapses.

In the Johns Hopkins Hospital Reports, Vol. VIII, p. 437, a protracted case with three relapses is reported. The patient, a woman of 26, had a primary attack in June; her first relapse occurred early in September; her second relapse early in November, the onset being with arthritis, and her case was at first thought to be one of acute articular rheumatism; her third relapse consisting of a fever of 9 days without rose spots or a palpable spleen. Recovery was complete.

That the relapse is much milder and less fatal than the primary attack has long been noted. A most striking series of figures is given by Melville.<sup>5</sup> He saw 295 cases of typhoid fever, 23 or 7.79 per cent had relapse and all the relapsed cases recovered. Of the 295 cases 7 died, a mortality of 2.38 per cent.

There is now considerable unanimity of opinion as to what the terms "relapse," "recrudescence" and "intercurrent relapse" mean. A relapse is never caused by external and exciting causes alone, such as sudden emotion, overfeeding, visits of friends, etc., but it is due to a reinfection of the organism with the typhoid bacillus. Shattuck,<sup>6</sup>

<sup>1</sup> Med. News, Phila., 1893, lxii, 154-156.

<sup>2</sup> Quoted by Hunt. Pract., Lond., 1898, ix, 263.

<sup>3</sup> Lancet, Lond., 1890, ii, 120-122.

<sup>4</sup> Ueber Typhus-recidive. 8° Strassburg, 1893. Inaug. Dis.

<sup>5</sup> Brit. Med. Jour., 1901, i, 952-954.

<sup>6</sup> Bost. Med. & Surg. J., 1889, cxxi, 221-224.

spots or enlargement of the spleen. Thus dividing the illness into days we have:

Primary attack August 2 to September 2 .....	31 days.
Apyrexia .....	26 "
First relapse September 28 to October 3.....	5 "
Period of practically normal temperature.....	4 "
Second relapse October 7 to October 17.....	10 "
Apyrexia .....	3 "
Third relapse October 20 to October 26 .....	6 "
Apyrexia .....	5 "
First recrudescence October 31 to November 2.....	2 "
Apyrexia .....	9 "
Second recrudescence November 11 .....	1 "
Apyrexia .....	19 "
Third recrudescence November 30 to December 1..	1 "
Discharged December 15.	

There was a long interval between the initial attack and

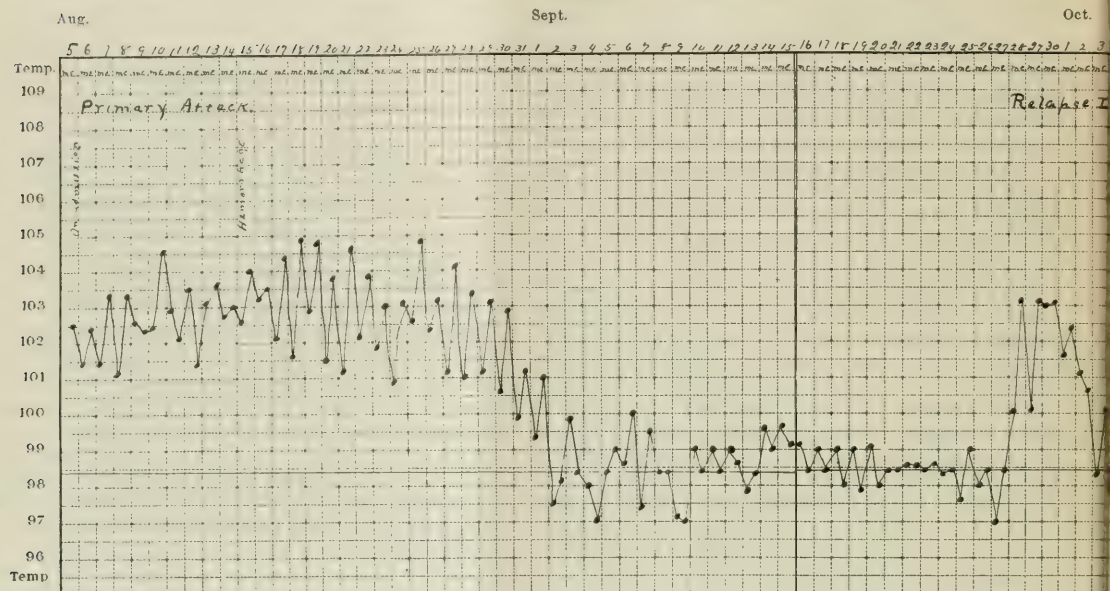
ulcers in the ileum and enlarged follicles in the colon; 3 cases without visible ulceration. Perforation occurred 10 times, the ileum being perforated nine times, the sigmoid flexure once. Of the 2 cases of relapse both had ulcers in the ileum, in one case healing in places. Neither case had an ulcer below the ileocecal valve. In other words, in two-thirds of the cases which died in the primary attack an ulceration of the colon was found. These figures show quite conclusively that such a theory as the one advanced above is inadequate to explain why relapses occur.

Within the past year a new theory of the etiology of the relapse in typhoid fever has been advanced by Durham.<sup>8</sup> When an animal dies with its blood containing a quantity of specific antitoxin substances he considers that its death may have been due to the action of some toxin or variety of toxin against which no antitoxin has been manufactured in the serum. He assumes that no infection is a simple process in which all organisms of the same species are iden-

<sup>7</sup> For large series of statistics see Béna, loc. cit. and R. Lohse, Ueber das Recidive des Ileotyphus. Freiburg i. Br. 1898.

<sup>8</sup> Relapses in Typhoid Fever. Pract. Lond., 1894, lii, 184.

<sup>9</sup> Jour. Path. and Bact. vii, 1901, p. 240.



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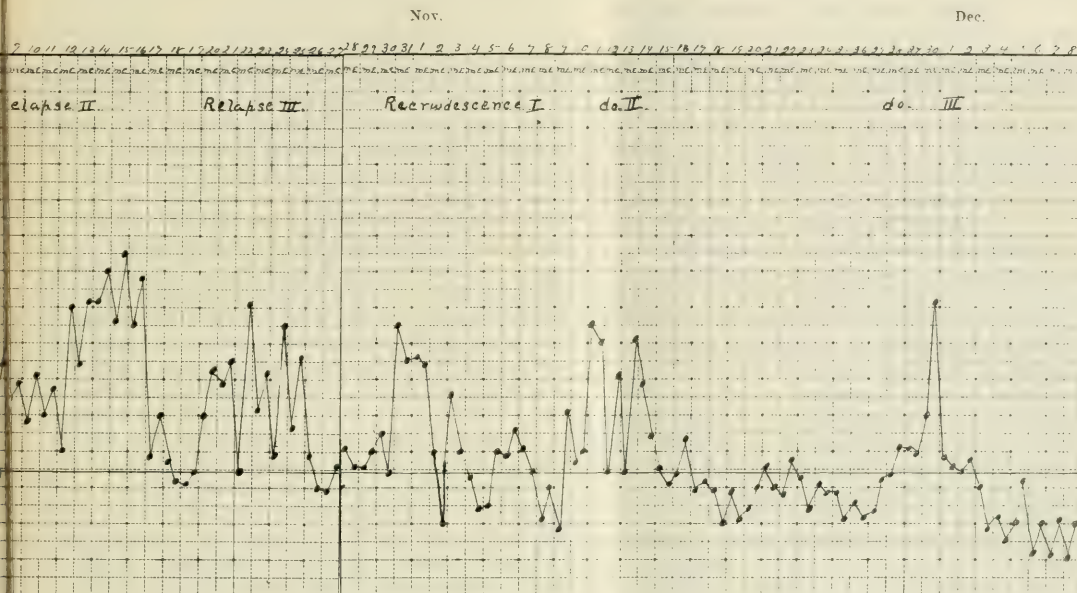
<sup>2</sup> Quoted by Hunt. Pract., Lond., 1898, ix, 263.

<sup>3</sup> Lancet, Lond., 1890, ii, 120-123.

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<sup>7</sup> For large series of statistics see Béna, loc. cit. and R. Lohse, Ueber das Recidive des Ileotyphus. Freiburg i. Br. 1898.

<sup>8</sup> Relapses in Typhoid Fever. Pract. Lond., 1894, III, 184.

<sup>9</sup> Jour. Path. and Bact. vii, 1901, p. 240.

to 14,500. Her leukocytes, which had, since the last rise, fallen to 7000, rose to 14,500. There were no rose spots but her spleen again became palpable. November 2, rose spots were seen on abdomen. Her temperature showed marked oscillations to November 4. She then appeared in good condition, was quite bright. There was considerable cyanosis of trunk and limbs although her temperature was normal. On November 7 a few fresh rose spots were seen, the spleen, however, was not palpable. There was an irregular temperature, at times reaching 102.6°, but on November 13, with this temperature and a rapid pulse, there were no fresh spots and her spleen was not felt. On November 18 her temperature became normal and remained so for 11 days. She was again apparently well and almost ready to go home. On November 30, the 121st day of her illness and 64 days since the first relapse, she complained of a headache. Her temperature was 100° at 6 a. m., rising at 2 p. m. to 103.7°. She was listless and apparently felt badly. Her pulse was 140, rather small; spleen readily palpable; no rose spots; abdomen natural, not tender. Her temperature remained elevated for 60 hours when it became normal and she passed

case was at first thought to be one of acute articular rheumatism; her third relapse consisting of a fever of 9 days without rose spots or a palpable spleen. Recovery was complete.

That the relapse is much milder and less fatal than the primary attack has long been noted. A most striking series of figures is given by Melville.<sup>5</sup> He saw 295 cases of typhoid fever, 23 or 7.79 per cent had relapse and all the relapsed cases recovered. Of the 295 cases 7 died, a mortality of 2.38 per cent.

There is now considerable unanimity of opinion as to what the terms "relapse," "recrudescence" and "intercurrent relapse" mean. A relapse is never caused by external and exciting causes alone, such as sudden emotion, overfeeding, visits of friends, etc., but it is due to a reinfection of the organism with the typhoid bacillus. Shattuck,<sup>6</sup>

<sup>1</sup> Med. News, Phila., 1893, lxii, 154-156.

<sup>2</sup> Quoted by Hunt. Pract., Lond., 1898, ix, 263.

<sup>3</sup> Lancet, Lond., 1890, ii, 120-122.

<sup>4</sup> Ueber Typhus-recidive. 8° Strassburg, 1893. Inaug. Dis.

<sup>5</sup> Brit. Med. Jour., 1901, i, 952-954.

<sup>6</sup> Bost. Med. & Surg. J., 1889, cxxi, 221-224.

discussing relapses, says: "Constipation, nourishment unsuitable in kind or too large in amount, the excitement of a visit, or a number of other causes may produce a return or an exacerbation (*what we call a recrudescence*) of fever: to produce a relapse there must be a re- or auto-infection."

There are certain well-known features of the relapse which may be mentioned. Chief of these are: (1) the shorter course; (2) the milder character as a rule; (3) a low mortality; (4) a more sudden rise of temperature, often reaching its maximum within 48 hours; (5) more often than not a rapid lysis. The fever of the relapse may be higher than that of the initial attack and the patient may be more severely ill. Whether the relapse which follows a severe attack is more severe or milder than one following a mild primary attack or vice versa it seems impossible to say. Nor can we predict from the nature of the primary attack whether or not there will be a relapse. Repeated efforts have been made to collect statistics to show that age, sex, race, time of year, etc., have some relation to relapses but the variations in statistics only show that no definite conclusions can be drawn.<sup>7</sup>

In the case reported the primary attack was severe. It was thought at one time that the bowel had perforated. Upon analyzing the various elevations in temperature it seems probable that the last three elevations were recrudescences rather than relapses. Although in the last one the spleen became palpable, still the transient elevation of temperature, its rapid fall and the rapid convalescence spoke against a true relapse. Also in one of the two short elevations preceding, there was a palpable spleen and a leucocytosis possibly due to cystitis. However, there was no coating of the tongue and the patient did not seem ill. In the recrudescence commencing November 11 it is probable that a soft boiled egg given on the afternoon of the 10th was the cause of a transient rise of temperature without fresh rose spots or enlargement of the spleen. Thus dividing the illness into days we have:

Primary attack August 2 to September 2 .....	31 days.
Apyrexia .....	26 "
First relapse September 28 to October 3 .....	5 "
Period of practically normal temperature .....	4 "
Second relapse October 7 to October 17 .....	10 "
Apyrexia .....	3 "
Third relapse October 20 to October 26 .....	6 "
Apyrexia .....	5 "
First recrudescence October 31 to November 2 .....	2 "
Apyrexia .....	9 "
Second recrudescence November 11 .....	1 "
Apyrexia .....	19 "
Third recrudescence November 30 to December 1 ..	1 "
Discharged December 15.	

There was a long interval between the initial attack and

the first relapse. A short but definite interval between the first and second, and second and third relapses and in the third relapse the temperature rose to within 4° F. of the highest temperature in the primary attack.

The question naturally arises why should a typhoid fever patient have relapses. Pneumonia, scarlet fever and diphtheria do not act thus. This question has attracted attention since Schultz in 1831 described three true relapses in 55 cases of typhoid fever which he thought to be due to overfeeding or exposure to cold. The relapse has been ascribed to one of two conditions, either (1) a second new infection, or (2) the result of the products of infection from the first attack remaining in the organism.

In 1894 Stewart\* (H. M.) collected and analyzed 40 cases of typhoid fever dead in relapse on whom autopsy was performed. He found that in 34, 85 per cent, of the cases the large intestine contained recent ulcers, while the small intestine showed the presence of recently healed ulcers. In the other 15 per cent there were ulcers both in small and large intestine. On the contrary, of 65 cases dead in primary attack 48, or 75 per cent, showed a healthy large intestine and ulceration in the small intestine. He thought that in the primary illness the small intestine bore the brunt of the attack while in the relapse the large intestine chiefly suffered. Hence he concluded that the relapse was due to a reinfection of the intestine by sloughs derived from some portion above.

The autopsy records of the Johns Hopkins Hospital were analyzed with regard to this point. 68 autopsies were found to March 15, 1902, of which 2 cases died during a relapse. Of 66 cases then there was ulceration in the ileum alone in 21 (31.8 per cent); in the colon alone in 1 case; ulcers in both small and large intestine were found in 41 (62.1 per cent), of which 3 cases had very slight ulceration in the ileum and extensive ulceration in the colon; 1 case with ulcers in the ileum and enlarged follicles in the colon; 3 cases without visible ulceration. Perforation occurred 10 times, the ileum being perforated nine times, the sigmoid flexure once. Of the 2 cases of relapse both had ulcers in the ileum, in one case healing in places. Neither case had an ulcer below the ileocecal valve. In other words, in two-thirds of the cases which died in the primary attack an ulceration of the colon was found. These figures show quite conclusively that such a theory as the one advanced above is inadequate to explain why relapses occur.

Within the past year a new theory of the etiology of the relapse in typhoid fever has been advanced by Durham.<sup>8</sup> When an animal dies with its blood containing a quantity of specific antitoxin substances he considers that its death may have been due to the action of some toxin or variety of toxin against which no antitoxin has been manufactured in the serum. He assumes that no infection is a simple process in which all organisms of the same species are iden-

<sup>7</sup> For large series of statistics see Béna, loc. cit. and R. Lohse, Ueber das Recidive des Ileotyphus. Freiburg i. Br. 1898.

<sup>8</sup> Relapses in Typhoid Fever. Pract. Lond., 1894, III, 184.

<sup>9</sup> Jour. Path. and Bact. vii, 1901, p. 240.

tical, but an infection is a complex phenomenon, due to the infection with the varieties and subvarieties of the infecting agent, no one of which being identical with nor equivalent to any other one. Should the groups be more or less equivalent we should have a normal, isozymic infection; should one or more varieties preponderate we should have an abnormal or anisozymic infection. Each variety and subvariety is then assumed to have its corresponding antibody formed in the blood.

This is quite consistent with and follows from the results of the recent work on hemolysis and bacteriolysis where apparently there are innumerable antibodies, everyone called forth by its specific toxin.

Durham says further that probably a pure infection never occurs, hence every infection consists of an infection with a number of varieties and the sum of the forces acting on the organism calls forth a quantity of responses and consequently a complex body is the result. If the different antibodies are called forth in sufficient number to take care of the toxins of the different varieties the organism recovers from the infection and no relapse occurs. If, on the other hand, the varieties are remote, there will be a preponderance of certain groups of antibodies which react only with the corresponding varieties of the infecting agent. There will also be a slight production of antibodies corresponding to the groups of the bacterium which have been, so to speak, overgrown. If, now, these latter bacteria start to grow, the organism will be reinfected as there are no antitoxins in the blood corresponding to these toxins. As these groups were fewer in number and were not so virulent as the groups causing the primary attack, so the relapse will be both shorter and of a milder character than the initial attack.

That this is not theory alone is borne out by numerous experimental observations and by analogy. It has been proved that there are differences in bacilli derived from the

same source by testing them with different sera.<sup>10</sup> Durham has shown<sup>11</sup> also that "not only are there quantitative variations in the amount of protective antibodies in the sera taken from typhoid fever convalescents, but also that there are apparently qualitative differences as well." These differences in the bacilli derived from the same source are too subtle to be shown in cultural media. It is only by their serum reactions that these differences can be made out and studied.

Again, we have a familiar example of variety in the behavior of the streptococcus. At one time erysipelas, at another time deep cellulitis, again rapid general infection and death may develop while culturally no differences can be shown in the cocci present. It has been repeatedly proved that every one of the numerous known varieties of streptococci has its own protective serum. Hence the divergent results obtained by those who have used antistreptococcal serum on patients infected with the coccus. The serum that would cure one patient would have no effect on another suffering from an infection due to a different variety.

It would seem therefore that Durham has sufficient grounds on which to base his hypothesis. The theory is more adequate than any yet advanced and as a working basis it suffices. On this theory multiple relapses can also quite readily be explained. For if every infection is complex, several groups of the infecting agent may cause the primary attack, several other groups the first relapse, several other non-identical groups the second relapse and so on. And the patient is liable to a reinfection as long as there are groups of the bacterium to counteract the toxic action of which no antitoxins have been formed in the blood or other tissues. It remains now for cumulative evidence to establish whether or not it is a pure hypothesis.

March 28, 1902.

<sup>10</sup> Pfeiffer and Kohl, *Zeitschr. f. Hyg. u. Infectious krank.*, Leipzig, 1886, Bd. xxi, S. 203. Quoted by Durham.

<sup>11</sup> *Jour. Path. and Bact.*, 1897, iv.

## THE CLINICAL VALUE OF OLIVER'S HAEMOCYTOMETER.<sup>1</sup>

BY WALTER BAUMGARTEN, A. B., M. D.

(From the Clinical Laboratory of the Johns Hopkins University.)

The object of this report is to call attention to certain sources of error in Oliver's haemocytometer, which indicate that it may be well to accept with some reserve the opinion that the instrument is satisfactory and accurate for estimating the number of red blood corpuscles in disease.

The construction of this instrument is based upon the fact that when a flame is viewed through a glass tube, it appears as a bright transverse line consisting of numerous small images of itself. When the tube so used is filled with a

fluid containing small particles in suspension, as for instance, red blood corpuscles, the interference with the transmission of light produced by them obliterates the line of images until a certain dilution of the mixture is reached. Oliver found that, using a tube of definite dimensions, a constant quantity of normal blood, and a definite diluting fluid, the point at which the line of images appeared could be determined within less than 1 per cent, and that the same was true for all variations in the number of corpuscles within normal limits. Taking 5,000,000 corpuscles as 100 per cent,

<sup>1</sup> Oliver, G., *British Med. J.*, i, p. 1493, 1896.

the tube was then graduated uniformly from this point to the bottom, which was taken as zero.

Oliver himself suggests the instrument as useful only in determining the number of red blood corpuscles in normal blood, and as applicable to physiological investigations rather than to clinical work in general. From the standpoint of the clinician he classes it with the haematocrit as a volumetric method, with which it shares the errors due to variations in the size of the corpuscle. In spite of the limitations so set upon it by Oliver, the instrument has been introduced into clinical work by others<sup>2</sup> with results which are alleged to agree very closely with actual enumerations by the Thoma-Zeiss instrument.

On putting the instrument to practical use in the clinical laboratory, Oliver's opinion as to its inadequacy in the anaemias was borne out, namely, that, compared to the Thoma-Zeiss count, its results varied as much as 20 to 30 per cent and more (both too high and too low). At Dr. Emerson's suggestion, and with his aid, the influence of certain elements of error entering into the determination was investigated.

In addition to the error due to variation in the size of the red corpuscles, an error is undoubtedly introduced by the coagulation of the proteids of the blood plasma by the mercuric chloride of Hayem's solution, which is used as the diluting fluid. Oliver minimizes this, and states that as much as 50 cmm. of serum, or five times as much as the blood-gathering pipette of the instrument contains, produces "the merest haze" when diluted to the 20 per cent mark. A repetition of this experiment gives in our hands a very different result, namely, a dense white coagulum is immediately formed, which interferes with the appearance of the reading until the dilution is carried to the 52 per cent mark.

Following this out, a single pipetteful of serum was substituted for the larger quantity. A series of observations so carried out demonstrated that a dilution with Hayem's fluid up to the 11 per cent mark was necessary to obtain a reading. This shows clearly that the coagulation of the serum causes an opacity which will be denser the smaller the dilution is, and will tend to disappear as the dilution is increased. The question arises, will this opacity increase the reading of the instrument above the point to which the corpuscles themselves would bring it.

In determining this question, mixtures of a normal blood (containing about 5,000,000 corpuscles per cmm.) and a freshly separated serum from human blood were made by drawing into the blood-gathering pipette varying proportions of blood and serum. Of three such mixtures, the first contained 20 per cent blood and 80 per cent serum, in which the reading should theoretically be obtained at the 20 per cent mark, representing 1,000,000 cells per cmm.; the second contained 40 per cent blood and 60 per cent serum, and

should be readable at the 40 per cent mark; the third contained 60 per cent blood and 40 per cent serum, and should read at the 60 per cent mark. The readings, however, were in the first mixture 7 per cent too high, corresponding to an error of 350,000 cells; in the second mixture 5 per cent, or 250,000 cells too high; while in the third mixture the error had practically vanished. This demonstrates that the coagulation of the proteids of the blood increases to some degree the extent to which the dilution must be carried to obtain the appearance of the transverse line of light, and that it forms a positive error.

In addition to the effect of the coagulation of the plasma, there is still another source of error, as Oliver has pointed out, namely, the variation in the size of the corpuscles. For example, even though the number of corpuscles be constant, the larger the corpuscles the greater will be the interference with the light, and the higher the readings obtained. Since the form of the corpuscles is such that changes in volume are due almost entirely to changes in area, and since the area varies with the square of the diameter of the corpuscle, the latter may be taken as an index of the changes in volume, and may be made the basis for calculation.

These two corrections, applied to actual cases, bring the error in the Oliver count, in most cases, within the limits of error of the Thoma-Zeiss instrument, taking this error at 200,000 cells. That the total correction is not more complete is probably to be ascribed to the fact that the graduating of the pipette used for the determination of the error arising from coagulation of the plasma, was crude; and it follows that the figures obtained by it are not perfectly accurate.

To illustrate the results obtained by Oliver's instrument, the following cases may be cited. The figures presented in the first two cases may be regarded as of more than ordinary value, as they are the results obtained from independent observations taken at the same time by a number of individuals; furthermore, they vary from the actual count within the limits of error of the Thoma-Zeiss counter.

TABLE I.		
Oliver.	Thoma-Zeiss.	Difference.
<i>Normal Case.</i>	Count.	
5,550,000	5,332,000	218,000
5,500,000		168,000
5,550,000		218,000
5,500,000		168,000
5,475,000		143,000
5,150,000		—182,000
5,200,000		—132,000
<i>Pernicious Anæmia.</i>		
Count I.		
3,900,000	1,725,000	2,175,000
3,675,000		1,950,000
2,850,000		1,125,000
2,850,000		1,125,000
Count II.		
2,800,000	1,256,000	1,544,000
2,900,000		1,644,000
2,750,000		1,494,000
2,775,000		1,519,000

<sup>2</sup> Cabot, *Clinical Examination of the Blood*, Fourth edition, 1901, p. 30.

Oliver.	Thoma-Zeiss.	Difference.
<i>Secondary Anaemia.</i>	Count.	
Case I. 3,050,000	3,600,000	—550,000
" II. 3,050,000	3,918,000	—868,000
" III. 1,650,000	2,120,000	—470,000

In a normal case with a Thoma-Zeiss count of 5,332,000 cells, observations were made with Oliver's haemocytometer by seven individuals, which varied from 5,150,000 to 5,550,000, differing from the count by from 132,000 to 218,000 cells. A case of pernicious anaemia with a count of 1,725,000 cells, gave results in the hands of four individuals varying from 2,850,000 to 3,900,000, a positive difference of from 1,125,000 to 2,175,000. The same case a number of days later gave a second count of 1,256,000 cells, while Oliver's instrument read from 2,750,000 to 2,900,000, an excess of 1,494,000 to 1,644,000. In the secondary anaemias Oliver's instrument gives results much below the count, as the three cases in the table demonstrate, namely, a deficit ranging from 470,000 to 868,000 cells.

The correction for the two errors has been made by subtracting from the result given by Oliver's instrument the error due to coagulation of the plasma at the reading in a given case, and then dividing the result by the factor representing the ratio of the square of the measured diameter of the corpuscles to the square of the diameter of the normal corpuscle, that is, of  $7.5\mu$ . Working out the first corrected case (pernicious anaemia) in this way (see Table II), the error due to plasma is 330,000, which, subtracted from the Oliver reading (1,150,000) leaves 820,000. The average measured diameter of the red corpuscles was  $8.7\mu$ .

TABLE II.  
Corrected Readings.

Oliver.	Thoma-Zeiss.	Difference.	Diameter	Corrected
	Count.		of Corpuscles.	Difference.
<i>Pernicious Anaemia.</i>				
1,150,000	798,000	+352,000	$8.7\mu$	—186,100
<i>Secondary Anaemia.</i>				
3,050,000	3,918,000	—868,000	$6.8\mu$	—198,500
1,650,000	2,120,000	—470,000	$6.8\mu$	—412,000

so that the ratio becomes  $\frac{8.7^2}{7.5^2}$ , giving the factor 1.34. Completing the correction, 820,000 divided by this factor gives 611,900 red blood corpuscles,

$$\left[ \frac{8.7^2}{7.5^2} = \frac{820,000}{x} \right] \quad x = \text{corrected reading,}$$

$$1.34x = 820,000 \quad = 611,900,$$

still leaving a difference of 186,100.

From the figures thus offered it may be seen that in the anaemias Oliver's haemocytometer gives very inaccurate results. The result is open to question in cases giving actual counts even as high as four million (3,918,000), so that this may be regarded as the lower limit of accuracy. Since readings above this point do not convey information of great consequence to the clinician, it may be concluded that Oliver's haemocytometer has very slight value in clinical work.

## THE BOYLSTON PRIZE.

Robert L. Randolph, M.D., Assistant Ophthalmic and Aural Surgeon to the Johns Hopkins Hospital, and Associate Professor of Ophthalmology and Otology in the Johns Hopkins Medical School, has recently received the Boylston Prize for a paper entitled: The Role of the Toxins in Inflammations of the Eye. An Experimental Study.

## NOTES ON NEW BOOKS.

Atlas and Epitome of Otology. By GUSTAV BRÜHL, M.D., of Berlin, with the collaboration of PROF. ADAM POLITZER of Vienna. Edited, with additions, by S. MACCUE SMITH, M.D., Clinical Professor of Otology, Jefferson Medical College, Philadelphia. With 244 colored figures on 39 lithographic plates, 99 text illustrations, and 292 pages of text. Cloth \$3.00 net. (Philadelphia and London: W. B. Saunders & Co., 1902.)

The latest and by no means the least valuable of the excellent series published by Saunders, this volume will receive a particularly cordial greeting because of the scarcity of otologic atlases. Those responsible for its appearance, however, have not depended upon this point to secure its appreciation, but have issued a work which commands the highest praise of those interested in the study or the teaching of otology. A well chosen illustration is valuable in the teaching of any subject and especially when dealing with anatomy does a clear and succinct demonstration enable the student to quickly comprehend the subject. A collection of illustrations such as lies before us is of great value also to the careful surgeon who finds it necessary to frequently refresh his memory of topographical anatomy. The temporal bone is by all odds the most difficult one in the human body to gain a complete and masterful knowledge of, and its variations in form and construction are so nearly innumerable as to require continuous study and constant watchfulness on the part of the operator.

Dr. Brühl appears to have had the privilege of choosing specimens *ad libitum* from Prof. Politzer's magnificent collection and he is certainly to be congratulated upon the excellent judgment displayed in his selections. The lithographic work has been most admirably performed and one can scarcely conceive any improvement upon it. The text descriptive of the figures is well arranged to bring out every point of importance in the illustration and render the whole perfectly clear. It is hardly necessary to speak of any plates in particular, they are all good, but those illustrating pathological conditions of the middle ear and its adjoining structures are perhaps the most important and the best prepared.

The second half of the book is a condensed treatise on diseases of the ear, intended especially for the student, and the author has succeeded marvelously well in compressing a comprehensive knowledge of his subject into the smallest space. In the main we agree with the opinions expressed and the advice given. A few minor mistakes appear, mostly misprints, as for instance, on page 67 the range of audition is given as from 16,000 to 50,000, when it was probably meant to state that the lower tone limit was 16; on page 70 the statement that "childhood and work in the open air predispose to inflammatory disease of the internal ear" should refer to the middle ear; and, on page 122, brain abscess is probably meant where the mortality of suppurative otitis media through "brain tumors" is spoken of. We cannot agree with the author in the limitations placed upon the use of the Eustachian

catheter. Personally, we incline to reverse his rule and use catheterization in preference to Politzerization whenever possible; the method is cleaner and the results more accurate.

We are very much gratified to note the endorsement given to the employment of formaldehyde in the treatment of suppurative otitis. Since reporting our own work with this agent we have continued to employ it in the majority of both acute and chronic cases with increasing satisfaction. Considerable space is devoted to the surgical treatment of diseases of the ear, especially for the cure of chronic suppurative conditions, all of which we heartily endorse. The importance of removing such foci of danger and thus avoiding the possibility of intracranial complications is well set forth, the indications for operation are pointed out and the methods of operating clearly described.

H. O. R.

Atlas and Epitome of Special Pathologic Histology. Vol. II.

By DOCENT DR. HERMANN DÜRRCK, Assistant in the Pathologic Institute in Munich. Authorized translation from the German. Edited by LUDVIG HEKTOEN, M.D. With 123 illustrations on 60 lithographic plates. (Philadelphia and London: W. B. Saunders & Co., 1901.)

No adverse criticism of this book seems to be justified. It is a compact book, well printed on good paper and full of colored illustrations which are really illustrative of the lesions they are intended to represent. These illustrations are drawn with care and clearness such as to make them immeasurably superior to the pictures in some of our recent American publications. The text is in places very concise and inadequate but for the great part it is written in a clear, fluent, literary style which leaves the student with a definite idea of the changes described and with energy to read more.

As the title indicates, the scope of the work is limited to the description of histological changes, but notwithstanding this fact it forms a book which ought to rank in the estimation of the student at least as high as any text-book of pathology published in English.

An American Text-Book of Pathology. Edited by LUDVIG HEKTOEN, M.D., Professor of Pathology, Rush Medical College, Chicago; and DAVID RIESMAN, M.D., Professor of Clinical Medicine, Philadelphia Polyclinic. 8vo. volume of 1245 pages and 443 illustrations. Cloth, \$7.50 net. (Philadelphia and London: W. B. Saunders & Co., 1901.)

It is of course to be expected that a large volume treating of pathology in general, and written in chapters by a number of different men, would be very uneven in its value from chapter to chapter. This general statement is well borne out in the book before us. It is divided into two parts, in the first of which several chapters treat of general pathology while in the second many more chapters treat of special pathology. It is impossible to enter into a detailed criticism of the work. The introduction is in the form of a general discussion of health and disease and touches on most of the fundamental principles of biology, concluding with some general advice to the student. Its lofty tone is in rather marked contrast with the rest of the book, many chapters of which seem to have been written in a perfunctory way, subjects being treated as if merely in fulfilment of the contract.

The chapters on general morbid processes, the osseous system, and the ductless glands are uniformly scholarly and are gracefully written. The difficult subject of tumors in general is treated in a thorough and comprehensive way and the relative values of the various theories with regard to them are carefully weighed. Objection may be raised to the use of the

name placentoma to describe those tumors to which so many names have been applied.

Teratology is presented clearly and in an interesting way, although it seems that the use of the terms genus and species in classifying various malformations is by no means justified since they are not in any way analogous to genera and species as the terms are ordinarily used. The illustrations in this chapter are good.

The discussion of leukaemia and Hodgkin's disease is very unsatisfactory and will probably be influenced in another edition of the book by the more recent literature.

The chapter on the digestive system is distinctly below the standard maintained in some other parts of the book. It seems to be based on a rather limited acquaintance with the literature—the Montreal Medical Journal seeming to be the principal source of information—but in spite of this, wide generalizations and classifications of the most unstable type are introduced. In places the author is also rather obscure as, for example, when he says that the omentum "being a variable organ at least almost absent, was looked upon as of comparatively little use." He then describes it as a "sort of nervous heart in the abdominal cavity which keeps up an imperfect form of circulation," and further leans to the idea that it is "useful to preserve the innate heat of the body."

The illustrations throughout the book are wretched—especially is this true of the colored drawings and many of the zinc plate reproductions, from which absolutely no idea of the real appearance of the lesions is obtained. The colored drawings for example on pp. 796, 866, 933, 947 are completely valueless. Photographs of gross specimens where they are used are of course good and there are many fairly good cuts copied from other works. The book is marred throughout by the grotesque spelling which has recently been affected by certain non-literary American medical publishers.

On the whole, although there are many good chapters, some being really admirable, it seems a pity that with such an expenditure of energy the book has not made any real advance over others already on the market.

Outlines of Physiology. By EDWARD GROVES JONES, M.D., Lecturer on Physical Diagnosis in the Atlanta College of Physicians and Surgeons, and Professor of Physiology in the Dental Department of the same. With 107 illustrations. 12mo., 400 pages. Price, \$1.50 net. (Published by P. Blakiston's Son & Co., 1012 Walnut St., Philadelphia.)

"This volume has been prepared with the view of presenting in as convenient form as possible the essential facts of modern physiology as related to the practice of medicine. In the execution of this purpose brevity has been made a prime consideration."

The four hundred pages of subject matter are divided into eleven chapters. Many of these are quite good. This applies especially to the chapters dealing with the cell (written by Dr. Frank K. Boland) and with nutrition. Occasional misstatements occur in these chapters but they fade into insignificance when compared with those that occur in some of the other chapters, especially those dealing with the chemical composition of the animal body and the senses. The author's attempt to bring the terminology of chemistry taught by our grandfathers into relation with modern chemical terms is probably the weakest feature of the work.

It is difficult to discover the place this book is to occupy. So far as brevity, "the prime consideration," is concerned we have already several text-books of physiology much more condensed than this four hundred page volume. And few of these brief text-books can boast of the inaccuracies that stud the

pages of the volume under consideration. It is to be hoped that a revision of the book will soon be undertaken, for it would give the author an opportunity of culling out the errors and of bringing the chemistry abreast of the times. This would make the book of greater value to the class of students for whom it evidently is intended.

A Practical Guide to the Administration of Anesthetics. By R. J. PROBYN-WILLIAMS, M.D., Senior Anesthetist and Instructor in Anesthetics at the London Hospital. (London, New York and Bombay: Longmans, Green & Co., 1901.)

This handy book of 200 pages is indeed all that its author intended it to be. It is well arranged, containing chapters on the "General Consideration of the Administration of an Anesthetic," "Difficulties and Dangers of Anesthesia," "Choice of the Anesthetic," and separate chapters devoted to nitrous oxide, ether, chloroform, and the mixtures, and on local anesthesia.

The chapter on ether is especially commendable, giving as it does all the main features of ether narcosis and the various phenomena that are likely to present themselves. We agree with the author in the stand he takes against the "open" method of administration as compared with the closed system, although we must confess that our experience with the latter method has been somewhat limited.

Nitrous oxide is fully considered but not given as wide a scope as we think possible. The writer does not tell us of its use along with air in prolonged and occasionally in even major operations. We think that this combination will become more popular and will be used more extensively in the longer surgical procedures, especially in very weak and ill patients with whom the strain of ether narcosis or the possible dangers of chloroform are to be avoided.

We regret that ethyl-bromide and chloride have not been mentioned as general anesthetics—not that we sanction their employment but that a few words on the author's experience with their use would be appreciated.

Considered as a whole, the book is clearly and concisely written and gives the reader as definite conceptions of the subject as reading matter can. It certainly must prove invaluable to students as it supplies "all the essential points in as small a form as possible."

MAURICE RUBEL.

Directions for Class Work in Practical Physiology, Elementary Physiology of Muscle and Nerve and of the Vascular and Nervous Systems. By E. A. SCHÄFER, LL.D., F.R.S., Professor of Physiology in the University of Edinburgh; formerly Jodrell Professor of Physiology in University College, London. With diagrams. (New York, London and Bombay: Longmans, Green & Co., 1901.)

This little book of seventy-five pages contains directions which are "based upon an experience of many years in University College, London," and which have been "printed for the convenience of" Prof. Schäfer's "Edinburgh students."

As is usually the case with most laboratory manuals in physiology, this book deals almost exclusively with the physiology of muscle and nerve. The physiology of the vascular and nervous systems, the only other subjects considered, occupy but one-fifth of the book. However, the subject is handled with such simplicity and clearness as to make it quite certain

that students will find it of considerable assistance to them in laboratory work. The most important features are the rough and ready character of the apparatus described, the lucidity of the numerous diagrams and the good judgment displayed in the choice of the experiments. These points may make the book of aid to teachers of physiology in planning laboratory courses.

## BOOKS RECEIVED.

*Essentials of Physiology.* Prepared especially for Students of Medicine. By Sidney P. Budgett, M.D. Arranged with Questions following each Chapter. Illustrated. (Saunders' Question-Compends, No. 1.) 1901. 12mo. 233 pages. W. B. Saunders & Company, Philadelphia and London.

*Outlines of Anatomy.* A guide to the Methodical Study of the Human Body in the Dissecting Room. By Edmund W. Holmes, A.B., M.D. Second edition. 1902. 16mo. 185 pages. The New Era Printing Company, Lancaster, Pa.

"*First Aid*" to the Injured and Sick. An Ambulance Handbook. By F. J. Warwick, B.A., M.B. Cantab., M. R. C. S., L. S. A., and A. C. Tunstall, M.D., F. R. C. S. Ed. 1901. 16mo. 232 pages. W. B. Saunders & Company, Philadelphia and London.

*Atlas and Principles of Bacteriology and Text-Book of Special Bacteriologic Diagnosis.* By Prof. Dr. K. B. Lehmann and R. O. Neumann, Dr. Phil. and Med. Authorized translation from the second enlarged and revised German edition. Edited by George H. Weaver, M.D. In two volumes. Part I, Atlas. Part II, Text. 1901. 12mo. W. B. Saunders & Company, Philadelphia and London.

*A Laboratory Course in Bacteriology.* For the use of Medical, Agricultural and Industrial Students. By Frederic P. Gorham, A.M. With 97 illustrations. 1901. 8vo. 192 pages. W. B. Saunders & Company, Philadelphia and London.

*A Text-Book of Pharmacology and Some Allied Sciences.* (Therapeutics, Materia Medica, Pharmacy, Prescription-Writing, Toxicology, etc.) By Torald Sollmann, M.D. Illustrated. 1901. 8vo. 894 pages. W. B. Saunders & Company, Philadelphia and London.

*The Principles of Hygiene.* A Practical Manual for Students, Physicians and Health Officers. By D. H. Bergey, A.M., M.D. Illustrated. 1901. 8vo. 495 pages. W. B. Saunders & Company, Philadelphia and London.

*An American Text-Book of Pathology.* For the use of Students and Practitioners of Medicine and Surgery. Edited by Ludvig Hektoen, M.D., and David Riesman, M.D. With 443 illustrations, 66 of them in colors. 1902. 4to. 1245 pages. W. B. Saunders & Company, Philadelphia and London.

*Nothnagel's Encyclopedia of Practical Medicine.* Variola, Vaccination, Varicella, Cholera, Erysipelas, Whooping Cough, Hay Fever. By H. Immermann, Th. von Jurgensen, C. Liebermeister, H. Lenhartz, G. Sticker. Edited, with additions by John W. Moore, M.D., F. R. C. P. Authorized translation from the German, under the editorial supervision of Alfred Stengel, M.D. 1902. 8vo. 682 pages. W. B. Saunders & Company, Philadelphia and London.

# BULLETIN

## OF

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## TRANSACTIONS OF THE HARFORD MEDICAL SOCIETY, 1797-8.<sup>1</sup>

BY EUGENE F. CORDELL, M. D.

Packard, in his recent History of Medicine in the United States, says that up to the year 1800, but 17 medical societies had been instituted in this country. In his list I find no mention of two that existed in Maryland in the 18th century, viz.: the Baltimore Medical Society of 1788-90 and the Harford Medical Society, founded in 1797. I have the pleasure of exhibiting to you a MS. volume of Transactions of the latter, the property of the Medical and Surgical Faculty of Maryland. It comprises 319 pages quarto, consisting of papers read by the members from April 1, 1797, to February 17, 1798, inclusive.

The society consisted of John Archer, M. B., and his pupils at "Medical Hall," his country-seat in Harford County, and its object was "mutual improvement by the perpetuation of important facts and the encouragement of well-regulated disputes."

In the preface, written by Robert Harris Archer, who seems to have been the leading spirit of the "confederation," bearing date March 28, 1798, we are informed that one of the early regulations forbade the reading of its papers out of the meetings; but it being found "that many cases were brot forward which were not only new but from which

some useful practical inference might be drawn," this idea was abandoned, "the pleasure which arises from doing good taking the place of modesty and diffidence, \* \* \* *non sibi sed toti* becoming a favorite maxim" of the members. The preface concludes: "If the reader should obtain no improvement from a perusal of the succeeding pages, it is hoped the disappointment will not produce declamation: a well-designed intention ought to shelter from the shafts of the satirical sneerer."

The membership, as given, consisted of eight resident members and one corresponding member. The former arranged in the order of their seniority were John Archer, M. B., President; Robert Harris Archer, Secretary; John Archer, Jr., M. D., James Walker, James Archer, M. D., William Harris, George Washington Archer and Thomas Bayer, the seven last named being pupils of the first. The corresponding member was Thomas Archer. I find that three of the papers were written by another person, A. Clendinen, whose name must therefore be added to those given above, making ten in all.

Of the above, John Archer, M. B., b. 1741, d. 1810, is well-known as the first medical graduate of the first medical school in the United States, viz.: that of Philadelphia; a native of Harford County, a master of arts of Princeton, a

<sup>1</sup> Read before the Johns Hopkins Hospital Historical Club, March 10, 1902.

patriot and statesman of the Revolution, a practitioner and teacher of medicine of high repute, a founder of the Medical and Chirurgical Faculty of Maryland and a member of Congress. The other Archers were his sons. At this time he was 56.

Robert Harris Archer, b. 1775, d. 1857, was also a native of Harford. He attended the University of Pennsylvania, but did not apply for the degree. He practiced successively in Baltimore from 1798 to 1805; in Lancaster, Pennsylvania, from 1805 to 1809, and later in Cecil and Harford Counties. He held the offices of member of the Legislature and of the Governor's Council and Judge of the Orphans' Court. He was now 22 years of age.

John Archer, Jr., b. 1778, d. 1830, M. D. of the University of Pennsylvania in 1798 and Surgeon of the Maryland Militia in the War of 1812. He died in Baltimore. He was 19 years old.

I find the name of James Walker as a graduate of the University of Pennsylvania in 1797. He is credited in the catalogue to Virginia. In one of his articles he tells us that he was 21 years old and of a delicate constitution.

James Archer, b. 1779, d. 1815, was born in Harford County, took M. D. at the University of Pennsylvania in 1804, practiced in Harford County, removing to Mississippi in 1810, where he died in 1815. He was 18 years old.

William Harris was a nephew, as well as pupil, of Dr. Archer, and lived at Sunbury, Pennsylvania. The name appears as that of a graduate of the University of Pennsylvania in 1812.

Of George Washington Archer we know nothing except that he died at the early age of 19, while still a student of medicine.

Adam Clendinen was a member of the Medical and Chirurgical Faculty of Maryland and died in 1829. There is an M. D. of that name in the catalogue of the University of Maryland in 1829, but doubtless of the next generation. The Clendinens were well-known physicians of Baltimore.

Thomas Archer, b. 1768, d. 1821, was born in Harford County, where he practiced and died. He attended lectures at the University of Pennsylvania, but, like his brother, Robert Harris Archer, above mentioned, did not obtain a degree. He was an invalid for many years. He was an incorporator of the Medical and Chirurgical Faculty of Maryland in 1799. He was 29 years old, which doubtless accounts for his being admitted as a "corresponding" member.

According to Quinan's Annals, "Thomas Bayer, of Md., died in Tiffin, O., in 1835," which is all that I have been able to find out about him.

The "Laws" of the Society provide for a President, a Secretary and a Treasurer. The duties of these officers do not differ materially from those usually assigned to them. The President is to "constitute" the Society every other Saturday precisely at six o'clock. He has the privilege of speaking upon any subject under consideration and has

power to fine any member acting in a disorderly manner, not exceeding a half dollar for each offense. In his absence the members are to elect a chairman *pro tempore* "by lottery." The Treasurer is to collect fines and hold "stock," etc.

Membership is obtained by application and ballot and no thesis is required for admission.

Each member, in turn, is required to present a "dissertation" on some subject connected with medicine, chemistry, botany, natural history or agriculture; as a case from personal observation with comments, or an essay corroborating or confuting some medical opinion which influences practice, etc. Failure to comply with this requirement is punished by a fine of 5 shillings for each meeting at which a member continues delinquent.

Two dissertations are to be read at each meeting. Extraordinary meetings are to be held on the first Wednesday in each month for the sole purpose of amending the by-laws and choosing officers. Every member is to stand "erect" and address the President "uncovered," under penalty of "one-eighth dollar" for each offense. Members who refuse to comply with the laws or pay fines are to be expelled, and the word "expelled" is to be written opposite their names in the Law Book.

The following certificate was to be issued by the Secretary: "*Societas Medica Harfordiensis, Anno Domini MDCCXCVII constituta, omnibus qui hæc legerint SALUTEM. Viro ingenuo et doctissimo, quem in numerum nostrum accepimus cujus diligentiae indefessæ semper nobis gratificationi fuere, has literas libertissime donamus, atque eum omnibus, philosophiæ et medicinæ cultoribus solícite commendamus. In quorum testimonium sigillum nostrum cum nomine Praesidis subscripto praesentibus apponi fecimus.*"

The number of dissertations in the book is twenty, representing all the "resident members" except the President and Thomas Bayer. There is no contribution from the corresponding member. The twenty papers are distributed thus: R. H. Archer and William Harris, each four; James Archer and A. Clendinen, each three; John Archer, Jr., James Walker and Geo. W. Archer, each two.

The subjects discussed are very varied in character—misplaced, bilious, pneumonic and cutaneous fevers, pleurisy, peripneumony, gastritis phlegmonica, lepra, hepatitis, lues, amenorrhagia, the circulation of the blood, the catamenia, the influence of the moon and the operation of oxygen upon the human frame, two cases of convulsions, the Brunonian method of cure of indirect debility and inquiries as to the primary operation of pestilential fluids and effluvia. At the beginning attention was confined to cases, but in the last half of the volume general conditions and wider views are discussed.

I think it will interest you, as it has me, to go over some of the papers minutely.

The first case by Robert Harris Archer "exhibits by unequivocal marks *y<sup>e</sup>* misplaced state of fever," and taught

him never to give a name to a disease on his first visit when he could avoid it. "To see at first glance the character of many diseases it requires a Physician not only to be well acquainted with the Laws of  $y^c$  animal œconomy but to have a considerable fund of practical knowledge. You will say examine the state of the pulse; but there are diseases which are reckoned general in which  $y^c$  pulse is not materially deranged."

A young man was attacked the night of January 29th with most violent pains in the hypogastric region, extending up to the right hypochondrium; pulse natural. On the previous day he got his feet wet and complained a little but ascribed his disease "to ye debaucheries which he indulged at the celebration of an hymeneal union."

During the continuation of the pains he had a constant discharge of matter from the urethra commencing three hours after the beginning of the attack and "resembling a gonorrhœal discharge." A diagnosis of cystitis was made. There were no symptoms of general fever, and the heat of body was not increased. The tongue was a little discolored, the abdomen natural, the urine free and passed without pain. Bled one pint, but pain not mitigated and blood not inflammatory in appearance but perfectly natural. Hot flannels were applied. The pain abated in a few hours and he sat up, complaining of considerable debility but inclined to take nourishment. A favorable prognosis as to return was given.

Two days after, at the same hour a second paroxysm occurred, similar to the first and lasting twelve hours. He was bled as before. On February 26 there was a third and less severe paroxysm. The reporter says: "This regular 'tertian' recurrence 'darted a ray of light across his mind' and his 'ideas took a different turn.'" He now thought that in addition to the local inflammation he had an intermittent fever to deal with, which, however, did not affect the arterial system generally. The pains now seemed more "concentered" in his back "which assisted in forming a true theory of his disease."

In confirmation of its being a "misplaced state of Fever," he mentions the appearance of "an universal yellowness of his skin and tongue" after the third paroxysm. With this the severe pain abated. "This can only be accounted for," he says, "by admitting that the morbid action began to diffuse itself thro'out the whole arterial system, thereby taking off the distension from those vessels which at the onset seemed to sustain the whole force of the disease."

He was now given large doses of bark and there was no return of the "fits." The remedy occasioned a diarrhœa calling for opium. "Dr. Rush has established beyond all controversy the existence of such cases and calls them 'misplaced states of fever.'"

Of this condition Mr. William Harris, another member of the Society, in a later paper has this to say: "This distinction appears paradoxical as the term fever signifies that state of  $y^c$  sanguiferous circulation which is in a morbid condition. Now if the disease is not in this part but confined to another, I cannot conceive that it is fever at all but merely an affection of the part to which it is confined." So these young men were bold enough to differ even from the great Rush!

At the second meeting John Archer, Jr., M. D., reports

a case of "Pleurisy," in a negro man, aged 26, beginning after exposure, with chill, high fever and very acute pain in the right side extending to the shoulder. On the 3d day he was seen and was at once bled and blistered and this was repeated on the 4th, "every symptom calling loudly for the lancet." He now had nausea and headache, dry hacking cough with little or no expectoration, breathing labored, tongue bilious, bowels costive. A large dose of calomel and gamboge was given and nitric acid and decoction of seneka ordered with plentiful diluted drinks. Though the venesection made little alteration in the pulse, there was some relief to the pain. The blood on becoming cold showed every mark of violent inflammation. On the 6th and 7th days of his illness, he was bled again, each time 6j; notwithstanding, the pain was very severe. A large blister was applied, the bowels were kept loose with "Glauber's Salts," and antimonials with nitre administered every two hours alternating with neutral mixture. On the 8th day  $\frac{3}{4}$  xii of blood were drawn and on the 9th he was much better, "the action of the pulse being taken down in a very commendable degree, the pain much abated and breathing partly natural, expectoration much more free." On the 10th day he sat up, the fever having abated and appetite returning. On the 12th day he was walking about, with a good appetite, and required no more medicine. "Cured."

Of this case, he remarks, in conclusion: "It is altogether without ambiguity, every described symptom strongly showing it to be an inflammation of the pleura and adjacent membranes." Of the causes of the disease, he assigns exposure as the remote and an irregular convulsive action of the arterial system as the proximate "according to the accurate and celebrated Dr. Rush."

The third case by James Walker is an account of an attack of dysentery which he had himself.

The symptoms were headache, severe griping pain, tenesmus and the frequent passage of blood-stained mucus. A "Brunonian treatment" by opium and astringents failed to relieve him, but he was cured by purgatives and "the antidyenteric boluses well-known to the members of the society and for the discovery of which they were peculiarly indebted to their illustrious patron, with particular observance of the antiphlogistic regimen." At the end of ten days nearly every symptom of the disease had disappeared, but now "anxious once more to enjoy his friends and society he precipitately rushed forth into his former habit of living and intemperance" and the disease returned with its former violence. The Brunonian treatment was again had recourse to and persevered in for four or five weeks without avail. At length despairing of recovery, and loath to submit to the antiphlogistic plan, which apparently seemed worse than the disease, "he resigned himself into the hands of nature." Whereupon, by a moderate course of living, in about three weeks to his inexpressible satisfaction, every symptom of disease disappeared.

In the fourth paper William Harris describes

a case of bilious fever in a slender and delicate young lady of 20, who, at his first visit, had been ill for several days with violent pains in the head, stomach and back, a bilious tongue, a pulse full, quick and tense, eyes yellow and tender, face flushed, bowels costive. She was vomited and purged, given nitre, antimony, neutral mixture and sulphur, a blister was applied to her nape, and four repeated attempts made at venesection; but, fortunately for the patient, I imagine, the blood would not flow. All measures of treatment appearing to fail, and the fever continuing, a course of salivation was determined on and

effected by means of calomel, 2 gr. doses and opium. She spat to the amount of three half-pints daily for two weeks, the fever meanwhile abating. She now complained of toothache and sent for a man who professed the business of "Tooth-drawing," and was with difficulty dissuaded from having her teeth removed. Her mouth and jaws were very much swollen, almost to the extent of preventing speech; otherwise her symptoms seemed better, her fever having nearly disappeared and her appetite having returned.

From her great desire now to have her mouth cured, which she called her "worst complaint," Mr. H. was prevailed upon to give Flor. Sulph.  $\frac{3}{4}$  j, which gave great relief and caused the flow of saliva to cease. Soon after this cessation [this word is underscored], she relapsed and had more violent fever than before. Evacuants and depleting remedies failing to check the fever, a second course of salivation was resolved on. In six days a discharge of saliva set in and continued two weeks to the amount of one quart daily. Notwithstanding her now greatly debilitated state, her fever only having abated in slight degree, the mercurial treatment was continued in order to maintain the pyalism and jalap was given to alter the state of her bowels. A few motions succeeded, but shortly after she fainted and was seized with cramps and convulsions and a feeling of numbness over the entire body; her face was distorted and mouth drawn. Mr. H. was summoned in haste, it being night, and found her in an alarming condition, pulse imperceptible, eyes sunken, face pale and skin cold like those of a corpse. All hope of her recovery was abandoned, but with the desire to be doing something for the sake of appearances, she was placed in a warm bath and friction was applied, while internally she took gum opium and camphor. An hour later, the convulsions returned with hiccough and vomiting. "Epithems" of camphor and opium were now applied to her abdomen, with a blister to each arm, and mustard sinapisms to the soles of the feet. The alarming symptoms continued but great relief was experienced from a glyster which caused several motions. Stramonium, vol. alkali, opium and other stimulants and antispasmodics were given and the blisters and sinapisms to the legs and arms were renewed, and after a dose of ether she got relief and some sleep, the first for forty hours. She awakened much recruited and asked for something to eat, which she had not done for four days. The alarming symptoms, however, reappeared and Dr. Archer was himself summoned in consultation. It was Dr. A.'s opinion "yt the cramp might depend upon the state of her stomach abounding with acidity" and he advised creta alba as an absorbent. Immediate relief ensued on the adoption of this advice and return of the spasms was always prevented by a dose of the remedy. Her stomach became less irritable, a more nourishing diet was given and she rapidly gathered strength.

Mr. Harris remained in the belief that had she been bled freely the fever would have been checked in the beginning. He also thought that the sudden arrest of salivation by the sulphur before the fever had been entirely subdued by the mercury, was responsible for her relapse. I will not give you the lengthy reasoning on this case based as it is upon the meagre physiological and pathological knowledge of the day, but it seems to me that it would have been better in many cases to confess ignorance than to indulge in ill-founded, verbose and profitless explanations.

The fifth case by James Archer

was a delicate, nervous girl of twenty, who had been subject during the winter and spring to many slight indispositions—

accompanied with headache, fever and tense pulse—which were always followed by sure and speedy recovery upon one or two bleedings.

On April 8th she was attacked after exposure with headache, etc., for which she was bled  $\frac{3}{4}$  x. Aggravation of symptoms followed and conscious that this was owing to blood not having been drawn in sufficient quantity, Dr. A. again bled her within a short time to  $\frac{3}{4}$  x. The blood appeared natural. Notwithstanding, on the following day, she had in addition, pain in the side and frequent cough. A blister was applied to her side and kept on 14 or 15 hours, but "raised badly." On the 3d day, she was still worse, her breathing being short and difficult, pulse rapid. "Every symptom called for the lancet," and she was bled to Oj. On the 4th day she appeared much better, and after a purgative dose of calomel, she was put on gr.  $\frac{1}{12}$  doses of tartar emetic. In the evening, she relapsed. Although every symptom again strongly indicated venesection she refused to permit it to be done. On the 5th day, it being unsafe to postpone the use of the lancet, her frivolous objections were overcome and Oj of blood was withdrawn which exhibited the usual buffy coat. Her pain now left but she was in a state of debility with constant nausea. On the 6th and 7th, she took Peruvian bark with febrifuge drops and on the latter day the Dr. had the pleasure of seeing her drink "two large dishes of coffee." For several days, she suffered from severe headache and constipation, notwithstanding large doses of mercury, jalap and gamboge, but a purge of "10 & 10" on the 10th day, relieved these and all her other symptoms. In summing up he says, "by the repeated use of the lancet and cathartics, the *magnum domini dei* in inflammatory disease, I had the happiness of seeing my patient restored to health."

The sixth case—Gastritis Phlegmonica—by A. Clendinen, was that of

a young man who after taking a very large quantity of volatile alkali with suicidal intent, was attacked with violent epigastric pain and burning, vomiting and intense headache and delirium. His pulse was preternaturally slow. He was bled to  $\frac{3}{4}$  xviii, and given a purge of castor oil, after which he became easier. The pains returning he was given demulcent drinks and clysters. These measures failing and a repetition of the bleeding being declined, tho' "inconsistent with the general practice," two-grain doses of opium were prescribed, which gave temporary relief. On the 2d day, the paroxysmal pains had returned, the tongue was dry, the pulse irregular and he had chills with great thirst and delirium. Bleeding was again insisted on and again declined; the diluent drinks and clysters were continued. On the 3d day the pains being still considerable, he was bled to  $\frac{3}{4}$  xij, and given a purge of gamboge, after which the symptoms gradually abated.

The seventh case was one of Pneumonic Fever by Robert H. Archer.

A man forty years old, of vigorous body and health, suffered three successive seasons from severe intermittent fever, contracted while acting as overseer to workmen employed in digging a canal. He had forebodings of fatal illness, but no attention was paid to these until his attack early on April 3d with a severe chill, followed by high fever and drowsiness, pains in the chest, cough and difficult breathing. He attributed the attack to wading in water, while building a dam five or six days previously. He was convinced that it was only a return of his chills and was with difficulty dissuaded from riding ten or twelve miles to attend to business. On the fol-



"Medical Hall," the home of John Archer, M. B., Harford Co., Md. The original house of frame is the rear part of the residence. The large front part has been added since. John Archer's office in the foreground.

Eighth case—Lepra—Dr. John Archer, Jr., reports the case of

a child two years old, who shortly after birth, began to suffer with a disease of the scalp, strongly resembling the common eruption of children. In spite of domestic remedies he grew worse, the eruption began to spread, itched intolerably and exuded "a watery humor." Troublesome abscesses formed on the head, neck and jaws. Otherwise the child was astonishingly lusty and had a voracious appetite for the grossest food. Medicines without number were given without the least effect. He was salivated and externally a wash of corrosive sublimate was applied, and a pitch cap of tar, brimstone and lard was worn for some time—all to no avail. The little patient was now left to his disease which spread over the body and extremities. Then at the urgent request of the parents, the Dr. ransacked the library at "Medical Hall" from top to bottom, when accident led to the discovery of a curative agent. He learned that a child with a similar affection had been cured by swallowing daily a number of millet shot. Astonished at this, he reflected on it, and came to the conclusion that the result was due to the arsenic added to the shot to render it more brittle. Accordingly he began by giving a minute quantity of arsenic three times daily. Improvement set in in a short time and the child was entirely cured. As the symptoms

the case did not agree with any genus in Cullen's nosology A. designated it as "lepra."

The ninth case was one diagnosed as Hepatitis by Mr. Liam Harris.

A robust woman of 30 was attacked with slight pain in her right side and breast ten days previous to her delivery. On January 29th she was delivered naturally of twins and soon after her pains increased and Mr. H. was summoned on February 2d, four days after her delivery. He found her in a very feeble state, with severe pains in breast, side, head and epigastrium, and a choking sensation as of a ball rising in her throat. Her pulse was full and strong, inspiration was painful and she had a troublesome, dry cough. Blood-letting was recommended without delay, but the midwife and friends objected on the ground that she had lost much blood during her pregnancy, and a venesection in addition would debilitate her very much. To this Mr. H. replied that the objections were too trivial for notice, and that her complaint was of an inflammatory nature and her symptoms strongly called for VS. which he knew would give immediate relief. She was willing but her friends still urged their "vain, foolish and obstinate" objections, and he yielded although he knew that he would be held accountable for any unfavorable result. He satisfied himself with applying a blister and giving *bol. camp. anodyn.* *℥* sal. nitr. and antimony as febrifuges, some laxative pills *℥* gum assafoetida *gr. iij* every four hours. Next day the patient being no better, he insisted more strongly on VS. "I told them," he says, "that unless they would let me prescribe and follow my directions, my attendance would be of no use. However, my ambition being roused, not willing to let my patient die through the means of their ignorance and obstinacy, and the pulse thoroughly inviting me to take some blood from her, without any further delay or hesitation, I bled up her arm, opened a vein and took from her  $\frac{3}{4}$  *xvi* of blood which when cold made a very sizzly appearance. Not five minutes after the blood was done running from the orifice, she felt an alleviation of all her pains. So great was the anodyne effect produced by the lancet, that she soon went to sleep and rested much easier for several days." After some days she had improved so much that she desired a discontinuation of the physician's visits. He was recalled, however, on the 14th and found one of her lower limbs greatly swollen up to the hip, and a high degree of fever present. She was bled *℥j*, a blister was applied, a cathartic administered with nitre and antimony, the limb was bathed with liniment, and decoction of mullein and friction directed. She was again bled and the same remedies were continued with gamboge. No change being still apparent, digitalis purpurea *gr. j* twice a day was prescribed, under which, with the aid of occasional purgation the swelling rapidly disappeared. It had nearly subsided by the 26th and she was able to walk. At this time a decoction of swamp willow root bark was given "to add strength to the system."

The author attributes the "hepatitis" in this patient to alternate exposure to heat and cold as the remote cause, an explanation which is quite common in the volume. He attributes the affection of the lower limb to the hepatitis through sympathy, Dr. Rush having observed such cases; there is no suggestion of any connection with the labor. He is not quite certain to which one of the remedial agents employed he is to ascribe the cure, "but from their operation the complaint vanished and she is now through the divine assistance (and their operation) enjoying perfect health and able to dandle her young offspring upon those limbs which have [in part]

been *ye* subject of these pages, and endowed with power to walk with unmolessted vigor in the visitation of her neighbors and *ye* duty and employment of her house and family." He concludes with this *Nota Bene*: "Whether any preternatural discharge of urine was produced by or during *ye* operation of *ye* digitalis, I cannot undertake to say. Delicacy prevented my enquiring into *ye* subject, but from many circumstances I am of opinion it had that effect which I need not at present mention."

In the tenth paper, James Archer, at this time not quite 18, reports a case of Lues Venerea. We learn from his opening remarks that there was at this time a "Harford Hospital" and that his medical observations were limited to cases seen therein which were of the most inveterate kind. This hospital, probably some outbuilding attached to Medical Hall, does not seem to have been conducted in a very model way, as no punctuality was observed in following the directions of the attending physicians and from the openness of the house, the patients were much exposed to the inclemencies of the weather, which rendered it unsafe in many cases to exhibit medicines.

A negro girl, aged 20, acquired syphilis in the natural way, followed by suppurating buboes, leaving troublesome ulcers in the groin and elsewhere, which corresponded with Bell's description of the Venereal Ulcer. Getting worse notwithstanding treatment, she entered the hospital where she was put through a mercurial course, two grains twice a day with opium. For five or six weeks there was a daily discharge of about a pint of saliva. Although she improved under this, she refused to take any more mercury "notwithstanding the most urgent solicitation." She now grew worse, painful buboes formed in her armpits and an ulcer which she had previously had on her foot became horribly foul and caused the loss of three of her toes. This ulcer was treated with a strong solution of corrosive sublimate. The young doctor was now desirous of producing another salivation in spite of her weak condition, but the mercury ran off by the bowels and failed to act. He says: "She led a life far worse than any kind of death, through stench, corruption and the shame attending it, till at last her mangled and breathless carcase was consigned to that happy alternative, the grave." He expresses the opinion that mercury is an antidote to the syphilitic virus and thus cures the disease.

The eleventh case by James Walker, was that of

a woman aged 25, who at the time of her menstrual period, was attacked with a chill followed by fever, headache and pain in the lower part of the abdomen. She was bled,  $\text{Oj}$  and  $\text{O}\frac{3}{4}$ , two days in succession, given cathartics, nitre and senna with mullein fermentations and in six days was well.

The next case is one which Mr. Clendinen designates as "Cutaneous or misplaced State of Fever."

It was that of a man aged 70-80, who for some years had labored under "a febrile state of disease." In the autumn of 1793, after an attack of intermittent fever terminating in a very formidable abscess of the heel, he began to be tormented with an intolerable itching and burning of the body. Large quantities of small vesicles were frequently noticed, which dried after a time, falling off in dark, bran-like scales, leaving the surface reddened in spots. One of the remedies ordered

for him by a Dr. Chanlie had been "as much of the Sal. Glaubii as would lay on an eleven-penny bit once every morning for eleven mornings." Mr. C. first saw him professionally in March, 1797, when the symptoms were all aggravated, with anasarca swelling of his left leg and arm, slow, full pulse, sleeplessness and fever. He drew  $\text{z}\text{xix-xiv}$  of blood, gave a cathartic and inserted an issue in the left leg; locally he applied a solution of corrosive sublimate alternating with one of sacch. saturni. Bleeding was repeated from time to time with purgation. Under this treatment the symptoms improved and by May he had so far recovered as to require no more aid. Of the title which he gives to this case, he says: "The justness of this epithet appears in its having first discovered itself in the type of a common intermittent, its being then from improper treatment translated to the heel, where it produced an uncommonly distressing inflammation terminating in an abscess, the disappearance of which ushered in all the above-described symptoms." He then gives Rush's causes of these translations or misplaced states: "1. Local debility in the part affected; 2. increased excitability in the part, in consequence of this debility; 3. the morbid excitement induced in the part by the stimulus of distension from the blood and by the effusion of serum, lymph or red globules in the weakened and afterward inflamed part." In other cases agues, fevers and even pleurisies were said to have terminated in scabies and this in turn to have given place to them, returning however on the cessation of the fever.

This meeting was held June 26. The Society now adjourned until December 16, at which time Mr. William Harris continued the reading of papers by one on the Influence of the Moon on the Body in Producing Paroxysms of Fever, etc. The longest paper is one on the "Operation of Oxygene on the Human System," etc., pp. 52, by William Harris, who was *facile princeps* the logician of the "confederation." The first half of the volume is devoted exclusively to the report of cases with remarks thereon; in the latter half almost all of the papers deal with general questions in physiology and pathology. There is, for instance, an interesting discussion as to what part of the body pestilential fluids and effluvia first attack, one following Rush in claiming that it is the vascular system, another a Dr. Gardiner, in maintaining the superior claims of the stomach and intestines.

There are many more interesting points about this volume, which, as it were, takes us into the confidence of the young doctor of a hundred years ago and tells us of the state of his knowledge, of his view of disease and of his trials and triumphs. As you have seen, the lancet was his great weapon in combating the monster, disease—the *magnum donum*—I am not sure that he did not mean *maximum donum—dei*, as one of them calls it. The use of this was scarcely amiss, for all disease in his view was due to increased stimulation—increased excitability. With this—backed by his mercury, his cathartics and his blisters—he feared no foe. It is astonishing the perfect confidence he reposed in these agents. If he failed, it was because he had drawn too little blood; if there was a relapse it was because the salivation had not been continued long enough. It must have been a very satisfactory frame of mind—the

practice of medicine upon such simple principles—the duty so plainly laid out for them. Brunonianism—the doctrines of John Brown—had no place in their affections—with its direct and indirect debility and its universal stimulation. With them, following the lead of their adored Rush—it was “war to the knife and the knife to the hilt;” the enemy had to be gotten out on sight—bled out, vomited out, purged out, sweat out, clystered out—any way and every way that they could get at him and drag him from his lair. But oh! for the poor patient! How our sympathies go out for him as we see him in the hands of these pitiless young Sangrados—floating in his own gore, drenched with horribly nauseating decoctions and boluses, with foetid breath, and teeth ready to fall out, spitting a quart of saliva a day for weeks and months. Truly, are we not justified in questioning whether the patients would not have been better off if they had been left to the resources of nature, which as Hippocrates taught more than 2300 years ago and as we now well know, is not an enemy but a friend in sickness. But they thought differently in those days and it is related of the celebrated Dr. Potter of this city, that he said on one occasion: “if nature came in at the door, I should pitch her out of the window!”

We find many references to Rush—“the accurate Rush”—“the celebrated Rush”—“the Father of American Medicine”—“the illustrious sage.” Listen to these words of Robert Harris Archer: “My heart is ready to burst for want of words to express the overflowing of my Gratitude to that Being who has contributed so largely towards meliorating the condition of Man by lessening the general stock of his sufferings—even my thot’s are too poor to do justice to his abilities. Do not mistake me—my Gratitude is not at present offered to the SUPREME RULER of the UNIVERSE. ‘Tis to a Being, who altho’ his Genius and Usefulness might entitle him to the first rank among the Spiritual Servants of God, yet he is—a fellow mortal—your friend—my friend—the friend of all mankind.”

Adulation could not have gone further without worship. Had Rush lived in the old days, he certainly would have had a shrine and a niche on Olympus.

On the other hand, John Brown could not be kicked and cuffed about too much and yet his influence was acknowledged in the very attention paid him. One of the authors—the same R. H. A.—acknowledges that at one time he had been in the toils of this false prophet. There are also allusions to an “ingenious and immortal Gardiner” (alas for the evanescence of fame!), to Hippocrates, Cullen, Darwin (the Zoonomian), Bell, Leake, Dickinson, Physick, Desportes, Lind, Pringle, Hoffman, etc., but almost all the quotations are from Rush’s writings direct.

Like their elders, the young men were fond of theoretical discussions as one of them says: “Ye young Phylologist although doubtful of its veracity, fond of displaying his talents engagee in ye Dispute and with all ye pomp of Language supports ye new Theory.” But it was soon abandoned for

another; “within the short space of five years,” one of them says, “I have three times changed my ideas of the nature of fever.” Some may be magnanimous enough to consider this fickleness as inseparable from the unsettled state of knowledge a century ago, or even as indicating a commendable independence of thought.

At 11, 32, the brain is said to be composed of different compartments, an idea which if developed might have led to the doctrine of cerebral localization. At 11, 33, I was surprised to find a distinction made between a temperature sense and common sensation and each referred to its own nerve fibres. At 11, 35, each disease is said to have its own peculiar contagion, which will produce that and no other disease. Why did they not go a step further and say “living” contagion. At 11, 5, is the following vigorous description of a hysterical facies: “Such was the malice and malignity depicted in her countenance that her presence would have added new horror to the gloomy caverns of Hell!”

Lastly, in perusing this volume, I was especially impressed with the incompleteness and inexactness of observation as compared with the methods of to-day. There is, for example, an entire absence of chemical and microscopical examination and all artificial aids to the senses. There is no report of family, and but little of personal, history. The frequency of pulse and respiration and of discharge of urine and feces is never once stated in figures. When accompanying these young physicians in imagination to the bedside of their patients, one feels almost like crying out, “My dear young grandfather, just put your ear down upon that chest and hear the cry of a crippled mitral valve or listen here to the fine crepitation of a commencing pneumonia; tap yonder below that scapula and note the flat sound of a pleura filled with effusion, or come let us see if these tubercles cannot be made to give some echo of their presence above this clavicle; or tuck your thermometer under this armpit for a few moments and see how easy it is to ascertain with precision the degree of your patient’s fever!” But the times were not yet ripe for these things. Auenbrugger had gone unheeded to his long repose and the genius of Laennec and Wunderlich had not yet pointed the way to the stethoscope and thermometer.

These were really very bright and talented young men and we must not judge them too critically and by our standards alone. They were but the reflection of their age—an age which believed death to be impossible in infectious fevers where free ptialism had been established (Davidge) and which at this very time was approving the bleeding of a yellow fever patient twelve or thirteen times (Rush). They labored under the disadvantage of knowing naught of the natural course of disease. We may think that they were deluded and far gone from the true path, but we must acknowledge that they were earnest followers of their great teacher, acting well in the light they had, and we

cannot believe otherwise than with a "*mens sibi conscia recti*."

NOTE: Hoping to glean some further information regarding this Society or its members, I wrote to Dr. Geo. W. Archer, of Emmorton, Harford County, a son of the Secretary of the Society, and grandson of its President, and he has kindly sent me some interesting details. He knows nothing of the Society but what is contained in this volume, which was a gift from him to the Faculty.

Upon the death of his mother in 1774, John Archer, M.B., her only surviving child, inherited her estate. But shortly after, dreaming for several successive nights that the house was struck by lightning and burned to the ground, he was so impressed that he determined to erect another house a few hundred yards away. Accordingly selecting a very low situation, so as to avoid any danger from lightning, he erected there a two-story frame dwelling of medium size in which he and his family lived the remainder of his days. This was "Medical Hall. On the death of Dr. Archer's widow in 1815, the estate became the property of her youngest son, Stevenson Archer, afterwards M. C. and Chief Judge of the Court of Appeals of Maryland. He added to it a three-story stone residence, converting the old house into

a back building. He dying in 1847 it descended to his youngest son, also named Stevenson, and also later M. C. A few years ago it was purchased from him by a grandson of the Judge, Hon. Stevenson Archer Williams, lately State Senator, who still owns it. The old office—a one-story stone building with cellar and loft—where the students—of whom there were about 50 in all during the last quarter of the eighteenth century—read and held their meetings, has entirely disappeared, but a picture of the place taken while it still existed, has happily been preserved and will shortly be reproduced in a history of Harford County which my correspondent is now engaged in writing. The "Hospital" mentioned in one of the papers must, Dr. A. thinks, have been the County Almshouse, situated two miles from Medical Hall, "near the road from the present Churchville to Bel Air, whose sick certainly received the services of the old Dr. and his students as his ledgers amply show." Dr. A. recalls his father telling him of one of the students being terribly scolded by his preceptor for bringing away for dissection the head of a pauper who had died there. The building has long since disappeared and when, some 15 years ago, Dr. A. visited the locality he was unable even to identify its exact site.

## THE DOCTORS GUSTAVUS BROWN OF LOWER MARYLAND.<sup>1</sup>

BY EUGENE F. CORDELL, M. D.

DOCTOR GUSTAVUS BROWN, 1st, the first of the family to arrive in America, was born, according to statements in his own handwriting in his Book of Common Prayer and Bible, at Dalkeith, near Edinburgh, Scotland, on the 10th of April, 1689, and was baptized the same day. His parents were Gustavus and Jane Mitchelson Brown, and his paternal grandfather was the Rev. Richard Brown, of the Established Church of England, a graduate of the University of St. Andrew's and minister to Salton in Scotland in the reign of Charles I. This Richard was the son of David Broun, as the name, which was a numerous one, was formerly spelt. Nothing is known of Dr. Brown's education, either literary or medical. In the old prayer book above referred to, he wrote: "I came into Maryland May 1708." Dr. Toner gave the following account of his arrival: "When a youth of nineteen, he became a surgeon or surgeon's mate on one of the royal or king's ships that came to the Colony in the Chesapeake Bay in 1708. While his ship lay at anchor, he went on Shore, but before he could return a severe storm arose, which made it necessary for the ship to weigh anchor and put out to sea. The young man was

left with nothing but the clothes on his back. He quickly made himself known, and informed the planters of his willingness to serve them if he could be provided with instruments and medicines, leaving them to judge if he was worthy of their confidence. He began the practice of medicine at Nansemond, Md. He soon gained respect and succeeded beyond his expectations. He married into a wealthy family, made a large fortune and wishing to lay his bones in his own loved Scotland, returned there with his family and became possessed, by purchase it is believed, possibly by inheritance, of the lands he disposed of by his will. His wife became dissatisfied with Scotland, and he returned in 1734 to Maryland, where he had years before purchased the seat of Col. Lomax, called 'Rich Hill,' four miles from Port Tobacco, Charles Co."<sup>2</sup>

Dr. Brown married in 1710, Frances Fowke, two years his junior, daughter of Col. Gerard Fowke, of Charles County. By her he had 12 children, of whom one son and seven daughters survived her. She died on the 8th of November, 1744, in her 54th year. Dr. Brown took for his second wife, Mrs. Margaret Black Boyd, widow of an Irish gentleman and merchant of Port Tobacco. By her he had two children, a son and a daughter. The son was

<sup>1</sup> Read before the Johns Hopkins Historical Club, April 14, 1902. In the preparation of this paper the writer desires to acknowledge his great indebtedness to the "Virginia Genealogies" of Rev. Horace H. Hayden.

<sup>2</sup> Hayden's Genealogies.

Gustavus Richard Brown, M.D., the second of the three physicians mentioned in this sketch.

Dr. Brown acquired a large and lucrative practice in Charles County and was prominent in public affairs. He was one of seven Trustees appointed by the Assembly to fill vacancies in the list of school teachers of the Province. He was active in matters of religion and donated an organ to his parish church. He was one of the commissioners appointed to regulate the parishes of St. Mary's and Charles Counties. In 1729 he was one of those appointed to lay out "a town at the head of Port Tobacco Creek." He was a vestryman of his parish and in 1755 Associate Judge of Charles County Court.

He had a number of medical students at "Rich Hill," two of whom became his sons-in-law, viz., Dr. Michael Wallace, of King George County, Va., and Dr. John Key, of St. Mary's County, Md. The nine daughters of Dr. Brown, known as "the nine Miss Browns," also as "the nine graces," all grew to maturity. They are represented to have been very fascinating and had many suitors. All married and their descendants are to be found in the well-known Moncure, Turner, Scott, Wallace, Key, Stone, Blackburn and other Maryland and Virginia families. Four of them married ministers, one, Margaret, married the Hon. Thomas Stone, of Maryland, signer of the Declaration of Independence. It is an interesting fact, which Dr. Brown mentions in his will, that upon the marriage of all of his daughters, he required their husbands to secure upon them the property which they received from him as dower.

Dr. Brown died at "Rich Hill," suddenly of apoplexy, some time in April, 1762. His will, dated December 9, 1755, was probated May 12, 1762. In this document he speaks of himself as "Practitioner in Medicines and Laird of Mainside and House Byers in Scotland," and refers to his lands of "Easter House" and his farm in and about Newstead, Scotland, and to his plantation called "Middleton," in Durham Parish, Charles County, Md. He provides most liberally for the education of his son, Gustavus Richard Brown, and directs that a mourning ring be given "to each worthy friend," naming seven persons thus designated. His Scotch property seems to have been given chiefly to his elder son Richard, whilst the younger received the main part of his Maryland lands. There are several codicils to the will. Mr. Thomas Swann, near Alexandria, owns portraits of Dr. Brown and his first wife.

The following anecdote—the only one that has come down to us—is told of him on the authority of his son-in-law, Dr. Wallace: "On one occasion Dr. Brown was sent for in haste to pay a professional visit in the family of a Mr. H., a wealthy citizen of King George County, Va., who was usually very slow in paying his physician for his valuable services, and who was also very ostentatious in displaying his wealth. In leaving the chamber of his patient it was necessary for Dr. B. to pass through the dining room, where Mr. H. was entertaining some guests at dinner. As Dr. B. entered the room a servant bearing a silver salver,

on which stood two silver goblets filled with gold pieces, stepped up to him and said, 'Dr. B., master wishes you to take out your fee.' It was winter and Dr. B. wore his overcoat. Taking one of the goblets, he quietly emptied it into one pocket, and the second goblet into another, and saying to the servant, 'Tell your master I highly appreciate his liberality,' he mounted his horse and returned home."

The indenture of Dr. Michael Wallace, one of the pupils and a son-in-law of Dr. Brown, is extant and is worth reproducing in this connection. This Dr. Wallace was born May 11, 1719, and died at his place, "Ellerslie," King George County, Va., in January, 1767.

#### INDENTURE OF DR. MICHAEL WALLACE.

Att Glasgow the Eighteenth Day of March One Thousand Seven Hundred and Thirty-four Years It is Contracted Indented and Agreed betwixt Lawrence Dinwiddie Merchant in Glasgow In Name and Behalf and for the Account of Dr. Gustavus Brown of Charles County in Maryland on the one part And Michaell Wallace Lawfull Son to the Deceast William Wallace of Galrigs with the Special Advice and Consent of Thomas and Michaell Wallace Merchts in Glasgow his Uncles And the said Thomas and Michaell Wallaces As Cautioners for their Said Nephew on the Other part That Is To Say the said Michaell Wallace With Consent for said Has Become Bound and Obligated and hereby Binds and Obliges himself to be an Apprentice and Servant to the said Doctor Gustavus Brown in his Bussiness and Imployment of Physick Surgery and Pharmacy Dureing the space of Six Years from his Entery Which is hereby Declared to be from his first and next Arivall in the said Charles County in Maryland During Which Space the said Michaell Wallace Junior as principall and the said Thomas and Michaell Wallaces his Uncles as Cautioners Bind and Oblidge them Conty and Severally their Heirs and successors that the said Michaell Wallace Junr. Shall Honestly Faithfully And Asidiously Serve and Obey the said Doctor Gustavus Brown his Master in his Bussiness and Imployment forsaid And all other his Lawfull Affairs Relateing thereto And Shall Attend him there Intill by Day and by Night and shall not Absent himself therefrom (Without Leave Asked and Given from his said Master or in Case of Sicknes) And that Dureing the space foresaid he shall forbear all Gameing Drinking and Keeping of Idle Company And shall not Dureing his said Apprenticeship have any patients of his own under Cure Upon No Pretence whatsoever. And that he shall not reveal his said Masters Bussiness and Secrets Nor the Secret Diseases of his patients And that he shall not Misbehave himself in any sort Nor Commit or Omitt Anything Contrair to the Meaning hereof And upon his failzieing in any of the Above points it shall be Lawfull for his said Master to Debar and Seclude him from his said service For The Which Causes On the Other part the Said Lawrence Dinwiddie Binds and Obliges Himself In Name and Behalf And On the Account of the said Doctor Gustavus Brown. That the said Gustavus Brown shall not only Teach Learn and Instruct the said Michaell Wallace his Apprentice In the Art of Physic Surgery and Pharmacy forsaid in every part and point thereof and to use his best and utmost Endeavour to make him Expert and Perfect yrin so far as he knows himself or the Judgement and Capacity of the said Michaell Wallace is Able to Uptake But Also to pay for his passage to the said County in Maryland And There to furnish provide and ent rtain him Dureing the space of ther Indentures In Meat Drink Cloathing Lodgeing and Washing And All Other Necessaries as becomes an Apprentice. Providing Always as

it is hereby Expressly provided and declared that in case the said Michael Wallace Apprentice for said On his arrivall in the said County in Maryland shall not Answer the Expectations of the said Doctor Gustavus Brown then it shall be Lawfull for him to Dismiss the said Michael Wallace from his Service Upon his Passage and Other Charges homeward to Scotland and in case the said Dr. Gustavus Brown should happen to Dye Dureing the space of this Indenture It is hereby Expressly Declared the same becomes Void and Null And the said Michael Wallace and his said Cautioners fully Discharged thereof and Both parties Bind and Oblidge themselves to perform and observe their Respective parts of the premises to Each Others Under the penalty of Twenty Pounds Sterling to be paid by the party failzier to the party observer or willing to observe the premises by and att our performance and the said Michael Wallace forsaid Binds and Oblidges me my heirs & to free Relieve and skaitheless keep my said Caurs of their Cautiong for me in the premises and of all Coast Skaith Dammadge and Expenses they may Sustain Therethrow Consenting to the Registration hereof in the Books of the Councill and Session or any others competent to have the Strength of a decreet that Lers. of Horning other Excells needfull may pass hereon and thereto Constitutes.

Ors prors. In Witness yrof thir presents Wryten on Stampt paper by James Bowman Wryter in Edinburgh Are Subscribed by us Place Day Moneth and Year of God Above Wryten before these Witnesses John Meek Maltman in Glasgow and the said James Bowman.

Law. Dinwiddie, Junr. Michael Wallace Thomas Wallace Mich. Wallace.

John Meek Witnes. James Bowman Witness.

The above Indenture is endorsed "Indenture betwixt Doctor Gustavus Brown and Michael Wallace 1734. June 6, 1740. Thos. , Michl Wallace compleated the words & time of the within Indenture given undr my hand the day & year as above. GUST. BROWN."

DOCTOR GUSTAVUS RICHARD BROWN, son of Dr. Gustavus Brown, 1st, by his second marriage, was born at his father's seat near Port Tobacco, according to his own statement, on the 17th of October, 1747. He was educated at the University of Edinburgh, where he took the degree of M. D. in 1768. His thesis, which was published in pamphlet form according to custom, was entitled "De Ortu Animalium Caloris," 8vo, pp. 45, Edinburgh, Balfour, Auld & Smellie, 1768. Among his fellow-students was the famous Dr. Benjamin Rush, of Philadelphia, who used to say of him that "he was not second to any student at the University at that period."<sup>2</sup>

After "walking" the London hospitals for several months, he returned to Maryland, stopping on the way for some time at the Medeira Islands and bringing thence with him a large collection of rare plants and flowers. As Dr. Craik was then practicing at Port Tobacco, he first settled at Nanjemoy, four miles distant, but the former moving later to Alexandria, he took up his residence at Port Tobacco, where he spent the remainder of his days. May 15, 1769, he married Margaret, or "Peggy," Graham, of Prince William County, Va., who brought him four children, viz.: Elizabeth, Margaret, Gustavus and Gustavus Richard. His daughters

died unmarried, but his sons left children and the name Gustavus is still perpetuated in Mr. Gustavus T. Brown and Gustavus R. Brown, D. D. S., both of Washington city, their descendants.

Dr. Brown was repeatedly solicited to take public office. He was a delegate from Charles County to the Maryland Provincial Council of 1774. During the Revolutionary period he was a firm and active patriot. At a meeting of the inhabitants of the county June 14, 1774, to protest against the act of Great Britain in closing the port of Boston, he was appointed on the committee of correspondence to call a general meeting and to correspond with similar committees in the other counties. He was one of the Judges of his county in 1776-7. It has been stated that he was a surgeon in the Revolution, but this is certainly a mistake. It may have arisen from his having attended some of the Continental troops at Port Tobacco. In the spring of 1776, in company with his nephew, Dr. James Wallace, he established a hospital for inoculation, as will appear from the following advertisement, which appeared in the *Virginia Gazette*, published at Williamsburg, on the 28th of June:

CHARLES COUNTY, MARYLAND, June 15, 1776.

The subscribers have fitted out & provided with every necessity a commodious house for the purpose of inoculation, where they are ready to receive such as are inclined to take the smallpox at the rate of £5 Maryland currency each. The distance being a little more than five miles from any part of the Potomac River, between the town end of Fairfax, & the upper end of Westmoreland counties, in Virginia, will render it very convenient to the inhabitants of the included counties. Those who will favor the subscribers with their company may depend upon their utmost care & attention.

G. R. BROWN,  
JAMES WALLACE.

Such as prefer coming by water may do it very conveniently, as the house stands on Burdett's Creek only four miles from its mouth.

He was a member of the State Convention called to ratify the constitution of the national government in 1788. He was a Visitor to St. John's College in 1789 and Grand Master of Masons of Maryland 1797-99.

As is well known, he was called in consultation in Washington's last illness, by Drs. Craik and Dick; but the patient—who was also his personal friend and neighbor—was already marked for death at his arrival, which was only seven hours before the fatal termination, and the combined efforts of the three physicians were unavailing. According to Dr. Toner, this was not the first time he had been called in consultation at Mt. Vernon.

Dr. Brown died at his residence, "Rose Hill," after a short illness, and while he was actively engaged in professional work. The funeral services of the Episcopal Church

<sup>2</sup>Dr. James Wallace, son of Dr. Michael Wallace, of Ellerslie, King George Co., Va., studied medicine under his uncle, Dr. Gustavus Richard Brown, of Port Tobacco, was surgeon in the Continental Army (first in the 2d, later in the 3d Va. Regt.) and after the war settled in Jacksonborough, S. C., where he died without issue, Dec. 13, 1790.

<sup>2</sup>Dr. Sewell's Lect., Columbian Col., Wash., D. C., 1825.

were held at his house and his remains were followed to the grave by a large number of relatives and friends. His tomb can still be seen in the garden at "Rose Hill," bearing this inscription: "Sacred To the Memory of Doctor Gustavus Richard Brown. This tombstone is erected By his relict Margaret Brown In Memory Of her respect & affection, And also as a monument Of his skill as a Physician, And his learning as a scholar, Of his wisdom as a Philosopher, His patriotism as a citizen, And his generosity as a friend, Of his elegance as a gentleman, And his hospitality as a neighbour, Of his kindness as a master, His tenderness as a husband and parent, And of his benevolence as a man. He died the 30th of Sep 1804 Aged 56 years."

Like his father, Dr. Brown was a man of fine personal appearance, being over six feet in height and well proportioned. His manners were pleasant and affable and he was a well-read physician and a fine classical scholar. He was particularly fond of botany and cultivated with great care and success an extensive garden of rare flowers, not for their beauty only but for their medicinal qualities. It was the most extensive and artistic collection in the State, occupying a sloping lawn of some ten acres, with three terraces and interlaced with serpentine walks, bordered with box-wood, savin, juniper and other rare evergreens. His collection of plants had been gathered from all parts of the world and his home took its name from his rare and extensive collection of roses. He provided means of irrigation for the summer and a large hot-house for propagating plants and for the care of the more delicate during the winter. Dr. Toner states that Dr. Hosack, while a practitioner in Alexandria in 1791 was a frequent visitor to Dr. Brown and his garden and that it was there that he conceived the idea which he subsequently so successfully carried out of founding a public botanical garden in New York city.

Dr. Brown was a favorite preceptor with the young men of Maryland and Virginia who were studying medicine. From the close of the Revolution until his death, his office was filled with students. His house was large and elegant and his hospitality unbounded. He is said to have used but few remedies, but those "of the most efficient character." His estate was productive and profitable and his professional income considerable, so that he was able to indulge his taste for good living and his fondness for flowers. He is said to have been the most popular man in his community. He was known and revered far and wide, and few there were within forty miles whom he had not at some time attended or befriended. He was an earnest Christian and attended church as regularly as his constant professional calls permitted. He was a communicant and vestryman of the Protestant Episcopal Church and a liberal contributor to it.

Dr. A. Taylor Norris, of Long Green, Md., has recently visited the home of Dr. Brown and sends me a description of it. The house said to have been built by Dr. Gustavus Brown, 1st, in 1764 (?) is a large colonial mansion built of brick imported from England (?). Connected with it by a covered walk is another brick house which was used by

the Doctor as an office and for his medical school; there he received and trained ten young men at a time. A large, well-lighted basement was used as a dissecting room, and beneath this is a dark cellar which tradition asserts was the receptacle for the bodies used for dissection.

Mrs. Joseph Horner, of Warrenton, Va., owns portraits of Dr. and Mrs. Brown, and Mrs. Vernon Dorsey, of Washington city, has his Edinburgh diploma. His two sons both became physicians.

The following letter, written to Dr. Craik a few weeks after Washington's death, throws light upon that celebrated case for which the attending physicians were so sharply criticised:

PORT TOBACCO, January 2, 1800.

Sir, I have lately met Dr. Dick again, in consultation, and the high opinion I formed of him when we were in conference at Mount Vernon last month, concerning the situation of our illustrious friend, has been confirmed.

You remember how, by his clear reasoning & evident knowledge of the causes of certain symptoms, after his examination of the General, he assured us that it was not really quinsey, which we supposed it to be, but a violent inflammation of the membranes of the throat, which it had almost closed, and which, if not immediately arrested, would result in death.

You must remember he was averse to bleeding the General, & I have often thought that if we had acted according to his suggestion when he said, "he needs all his strength—bleeding will diminish it," & taken no more blood from him, our good friend might have been alive now. But we were governed by the best light we had; we thought we were right, & so we are justified.

Dr. Dick is a most sensible man. He uses his common sense instead of the books as his guide in his profession, & he is no bigot. He says our professional practice needs great reform, & that can be brought about only by each individual becoming a practical reformer himself. He is disposed to put up his lancet forever & turn nurse instead of Doctor, for he says one good nurse is more likely to assist nature in making a cure than ten Doctors will by his pills & lancet.—(Lossing's Hist. Rec., II, 506, quoted by Hayden.)

DOCTOR GUSTAVUS BROWN, 3d, was the grandson of Gustavus Brown, 1st, and, although some years older, the nephew of Gustavus Richard Brown, 2d. He was the son of the Reverend Richard Brown (a minister of the Anglican Church, born at "Rich Hill," December 2, 1825), and was born at "Mainside," near Edinburgh, in 1744. He studied medicine at the University of Edinburgh for seven years and obtained his degree there in 1770, the entry of his name and thesis in the catalogue of graduates being: "Brown, Gust., Brit., De Cynanche Phlogist., 1770."

He came to America shortly after in company with Drs. Henry Reeder (uncle of the lady whom he afterwards married), Lansdale, Ireland, and some say, Goldie, his fellow-students at Edinburgh, and with them settled in St. Mary's County, Md. Some say that he served in the Maryland Line during the Revolution, but I have seen no evidence of it. In 1782 he attended his friend, Dr. Ireland, and the illness proving fatal, married his widow. This lady, who was Susannah, only daughter and child of Col. John Reeder,

of the Revolutionary Army, and of a Huguenot family settled in Maryland in 1736, was very rich and lived on an estate called "Summerseat." Here the Doctor settled down after marriage and here he died on the 3d of July, 1801, at the age of 56. He left no children, but his wife had a daughter, Dicandra Ireland, by her first husband.

In the last illness of Washington, Dr. Brown received a summons at midnight to see the illustrious patient in consultation with Drs. Craik, Dick, and Gustavus Richard Brown. He mounted his horse and hastened towards Mt. Vernon, but when he reached Long Bridge, he learned of Washington's death and turned back. The hastily-written summons, together with other relics of Dr. Brown, were destroyed by fire at the old homestead in 1874.

Dr. Brown practiced with great success in St. Mary's County. To him, through his father, descended by entail the Scotch estate, but as he left no descendants, at his death it went to Gustavus Richard Alexander Brown, of William.

His remains were buried in the Reeder burial ground at Westfield, St. Mary's County, and his tombstone bears this inscription:

Gustavus Brown, M. D.,  
Native of Maiden Side, Scotland,  
Died July 3, 1801,  
Aged 56 years.

He was a good man—courteous, generous & hospitable in private life. In public character, humane & useful, skilful & unrivaled.

"If virtue, honor, wisdom  
May claim a grateful tear  
Reader, approach this silent earth,  
And pay that tribute here."

Both Gustavus Richard Brown and Gustavus Brown, 3d, were among the 101 incorporators of the Medical and Chirurgical Faculty of Maryland in 1799.

## A CONTRIBUTION TO THE HISTORY OF MEDICINE IN THE PROVINCE OF MARYLAND. 1636-1671.

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The history of medicine in the United States has been but little studied although it offers many inducements to investigators. Recently Packard<sup>1</sup> has collected valuable data bearing on this subject and Thacher,<sup>2</sup> Beck,<sup>3</sup> and Toner<sup>4</sup> have also worked somewhat in this field. They all give but little information about early Maryland medicine.

The publication of the Maryland Archives by the State has opened a vast storehouse of knowledge about these early times and has drawn especially the late Dr. John R. Quinan, of Baltimore, to their study. His special articles are mostly to be found in the *Maryland Medical Journal*<sup>5</sup> and in his *Medical Annals of Baltimore*. It is to be regretted that he could not have undertaken a complete history of this period. Our paper, begun some years ago, has derived most of its material from the Maryland Archives.

Medicine at this period was in a somewhat chaotic state. Of the three classes of medical practitioners—the priest

physician, the regular physician and the empiric or charlatan—Maryland seems to have possessed but the second and last. No reference has been found to priest physicians who appear to have been so numerous in the history of the New England States.

Of the regular physicians nothing has been gained as to their preparation for the study of medicine nor have we been able to learn if any were graduates from medical colleges in the old world. "At that time medical practice was learned in apprenticeships; young men would serve and study with a practitioner from three to seven years and those who had the means, and the ambition of learning, went abroad to Leyden, Paris, Padua or Great Britain."<sup>6</sup> The doctors in these early times in the Province of Maryland are mostly styled in the records Physicians and Chirurgeons. One of their number is once called the Dutch Doctor,<sup>7</sup> but his name, Emperor Smith, does not suggest a Dutch origin. Another, George Binx, is mentioned in one place as a "Licentiate in physick."<sup>8</sup> We will speak more about him later. He performed the first autopsy in America of which we have any written report. Three early doctors (Purivant, Ellyson and Robinson) are called barber-chirurgeons, but one of them (Robinson) is more frequently dubbed barber.

<sup>1</sup> Packard, *The History of Medicine in the United States*. Philadelphia, 1901, pp. 542.

<sup>2</sup> Thacher, *American Medical Biography*. Boston, 1828, 2 vol. in 1, pp. 436 and 280.

<sup>3</sup> Beck, *An Historical Sketch of the State of American Medicine before the Revolution*. Albany, 1842, pp. 35.

<sup>4</sup> Toner, *Contributions to the Annals of Medical Progress*. Washington, 1874, pp. 118, and *The Medical Men of the Revolution*. Philadelphia, 1876, pp. 140.

<sup>5</sup> Quinan, *Illustrations of Medicine in Maryland in "Ye Olden Time."* Md. Med. J., 1883, X, pp. 51-52, 180-181, 275-276, and 324-327.

<sup>6</sup> Jacobi, *American Medicine*. Medical Record, N. Y., 1900, lviii, p. 201.

<sup>7</sup> Provincial Court, ii, p. 468.

<sup>8</sup> Provincial Court, i, p. 72.

Besides confining themselves to the practice of medicine, many found some time to devote to the public weal and at least eight of them served their Lord Proprietor as burgesses in the Assembly. Of this number Thomas Gerard is justly the most prominent. He came over in 1638 and settled on the Island of St. Clement in St. Mary's County. He was elected to the Assembly the following year<sup>9</sup> and served in it almost continuously till named as one of the Council November 17, 1643.<sup>10</sup> There he wielded vast influence. The Assembly which sat from February 28-March 14, 1659-1660, was convened at his house and at the house of Mr. Robert Slye.<sup>11</sup> In the troubles of 1655 he stood firm on the side of Lord Baltimore but in 1659, when Fendall tried to usurp power and the Upper House was dissolved, Fendall, Gerard and Utie<sup>12</sup> took seats in the Lower House and the two latter were then appointed to the Governor's Council. Gerard's loyalty to Lord Baltimore seems at that time to have waned, and he no longer appears prominent in public life after Fendall was deposed. For shortly thereafter Fendall and Gerard surrendered themselves, were indicted by the grand jury at the Provincial Court and, after trial, were found guilty of treason, receiving the sentence of banishment and confiscation of their estates. Both were subsequently pardoned by the Governor and Council "on each paying a moderate fine, forfeiting their privilege of voting and holding office and giving sufficient security for their good behavior towards his lordship and his government."

On April 30, 1640,<sup>13</sup> Cecilius, Lord Baltimore, appointed Gerard "conservator of our peace" for St. Clements Isle, Heron Isle and some adjacent territory. He long served as one of the Justices of the Provincial Court. He was a devout Catholic and his zeal caused him on one occasion "to take away the key of the Chappel" and to carry "away the Books out of the Chappel" so that the Protestants desired the Assembly to institute such proceedings against him for it as to Justice appertaineth. He was found "guilty of a misdemeanor and that he should bring the Books and Key taken away to the place where he had them and relinquish all title to them or the house and should pay for a fine 500 lbs. tobacco towards the maintenance of the first minister as should arrive."<sup>14</sup> Some time later a serious charge is recorded against him. He was charged with disclosing some of the Council's proceedings against his oath and as lacking in loyalty. They also accused him of intemperance on one occasion.<sup>15</sup> One witness, however, could not "swear that he was Drinke but that he had been drinking," while another deposed that Gerard "had drunke something extraordinary but was not so much in drinke but he could gett out of a Cart's way." The Assembly seems to have done

nothing regarding these charges although Gerard desired his actions to be looked into. He probably caused Lord Baltimore,<sup>16</sup> later, to write in a letter to Fendall, "yow shall doe well, if hee (Gerard) shall desire it from yow, to examine the complaints that are against him, and according to the meritt of the Cause acquitt or censure him."

We do not see much of his record as a physician in the Archives. In 1639<sup>17</sup> he obtained 230 pounds of tobacco from John Lewger, the Secretary of the Province, "for Physick" administered to Richard Lee. Doctors Gerard and Hooper appear to have attended Lee during his last illness, and they later testify how he would dispose of his estate as he left no will. One of the chief items was that he willed his wife's "sattin petticoate" to Mrs. Lewger and made her husband one of his executors."

It seems probable that Gerard early gave up the practice of medicine and devoted himself mainly to being Lord of St. Clement's Manor<sup>18</sup> and to the various official positions he was called upon to fill. He was a man of wealth and in the various assessments made for St. Mary's County and for the Province he was always assessed more than any other doctor. His name appears frequently in the Court records as suing and being sued, or as acting as a jurymen, administrator of estates, or an attorney. One instance will show his capacity as a lawyer. Robert Edwards<sup>19</sup> brought suit against him for not bringing him a good breeding sow at Christmas. Gerard testified that he bargained not for a breeding sow but for a "young sow ready to pigg or piggs by her side." Such an one he had tendered to Edwards at the proper time but he refused to take it. This defense seems to have been considered so plausible that the case was dismissed.

The other name we must mention as prominent in public life is that of Dr. Luke Barber. He appears with Henry Coursey<sup>20</sup> as mediator between the royalists and the puritans at Providence on March 23, 1655. He was then taken prisoner. On account of his loyalty at this time Lord Baltimore gives him "1000 acres of land at Porttobacco in case it appeare the said Coll: Yarly or his wife or his heires have no right thereunto."<sup>21</sup> Barber once served as deputy lieutenant<sup>22</sup> for six months while Fendall was out of the Province and was several times in the Governor's Council.<sup>23</sup>

The other legislators were John Robinson, Richard Purliant, Thomas Morris, Alexius Pulton or Putton, George Binx, Henry Hooper and John Wade. John Robinson<sup>24</sup> served but in one Assembly and we get but a slight glimpse

<sup>9</sup> Council, i, p. 384.

<sup>10</sup> Provincial Court, i, p. 107.

<sup>11</sup> Assembly, i, pp. 389-390. Johnson's Old Maryland Manors (J. H. U. Studies in Hist. and Pol. Science, 1883) gives the Records of the Court Leet and Court Baron of St. Clement's Manor, from 1659-1672.

<sup>12</sup> Provincial Court, i, pp. 135-143.

<sup>13</sup> Scharf, Hist. of Md., Balto., 1879, i, p. 218.

<sup>14</sup> Council, i, p. 325.

<sup>15</sup> Council, i, pp. 331-332.

<sup>16</sup> Council, i, p. 359 and elsewhere.

<sup>17</sup> Assembly, i, p. 116.

<sup>9</sup> Assembly, i, p. 29.

<sup>10</sup> Council, i, pp. 138-139.

<sup>11</sup> Assembly, i, p. 380.

<sup>12</sup> Scharf, Hist. of Md., Balto., 1879, i, pp. 267-268.

<sup>13</sup> Council, i, pp. 89-90.

<sup>14</sup> Assembly, i, p. 119.

<sup>15</sup> Council, i, pp. 354-357.

of him. He was later apprehended for debt.<sup>25</sup> Richard Purlivant was an early comer to Maryland and received "100 acres for having transported himself at his own charge into the Province, and two hundred more for having practiced his art to the benefit of the inhabitants of our Isle of Kent."<sup>26</sup> Thomas Morris was a burgess from St. Michael's hundred<sup>27</sup> in St. Mary's County. He was an early colonist in Maryland and served in two Assemblies. Alexius Pulton or Putton was also in the Assembly from St. Mary's County.<sup>28</sup> He is mentioned as having received in 1642 150 lbs. tobacco as surgeon's pay in the late expedition.<sup>29</sup> Again when Lewger paid Gerard 230 pounds of tobacco for Physick,<sup>30</sup> Pulton, who may have been called in for consultation, received 140 pounds. George Binx served in one Assembly.<sup>31</sup> His name is frequently in the Court records as suing for physick charges. On one occasion he sued "Nathan: Pope for 5 barrels of corne due for physick to Tho: Oliver,"<sup>32</sup> the debt's servant, and 2 barrels of corne more for labour and physick extraordinary to the said Tho: Oliver." Again he sues no less a personage than Sir Edmund Ployden,<sup>33</sup> the great grandson of Edmund Ployden, the eminent jurist, "for pains and physick last somer for cure" of one of his servants.<sup>34</sup> On another occasion the Court directs that the man owing Binx for physick should pay him 300 lbs. of tobacco and give him also a pap of powder.<sup>35</sup>

Henry Hooper we have referred to above. He appears a number of times in the records and seems to have had just the same difficulty in collecting bills as doctors now experience. On March 16, 1644,<sup>36</sup> he maketh oath "that he hath performed chirurgery for henry Lee, to the value of 100 lbs. tob., according to Justice and good conscience w<sup>ch</sup> yet is unsatisfied to him." Later he is bold enough to demand from his Lordship's attorney "3379 lb. Tob. and 3 lb. Corne due to him for his sallary and chirurgery in the flort of St. Inegoos the last yeare." His Lordship acknowledged 1559 lbs. of tobacco "as due for surgery and Physick to the soldiers during the time of the garrison. but for the other part of the demand he doth not find anything due unto him for the same."<sup>37</sup> The Court however thought differently and found for Hooper "500 lbs. tob." In 1650 he enters into an agreement with the Governor to serve him "for a twelve month from this day in the quality of Chirurgeon and the Governor is for it to find all druggs, and to find him with diett and lodgeing, and to allow him two thirds of all the accounts which the Chirurgeon Shall earn by his practice in the Colony during the Said time."<sup>38</sup> He seems

to have some military ability as he was made captain, in 1650, of one of the four military companies.<sup>39</sup> Somewhat later we learn Capt. Odbur is appointed in his stead as he was out of the Province.<sup>40</sup> In 1653 Ralph Crouch is mentioned as his executor.<sup>41</sup>

Of John Wade we have little information. His mark for cattle and hogs was both ears "flower deluced with Slits and the right ear underkeeled."<sup>42</sup> He appears in the Court records as appraiser of an estate, jurymen, witness, plaintiff and defendant. In 1650 he sued the estate of Thomas Medwell, whom he had transported as a servant from England, for 1080 lbs. of tobacco and cask.<sup>43</sup> In the itemized bill the medical charges are most interesting. They are as follows:

	lbs. Tob.
It for a vomitive potion for himself.....	20
It for breathing a vein for himself.....	10
It in another sickness at the fort for Physick and the botome with Dea phoretic and Sudoretick Cordi and Corobrotines for his Stomach and my pains (i. e. phlebotomy with diaphoretics, and sudorific cordial, and corroboratives. Browne).....	300
Itt in his last sickness more for 5 Cordialls Dormytine (dormitive).....	200
Itt for other Astringent means.....	150
Itt for visiting two times.....	250

Medwell never seems to have acted as servant for Wade and frequently desired him to take away the title of servitude. This Wade promised to do for satisfaction which he never got. He won the above suit and was also given by the Court 700 lbs. tob. for transporting Medwell out of England. Six years later Wardriff,<sup>44</sup> a servant, had Wade arrested for the non-payment of a year's wages. In this trial one witness testified that, besides curing Wardriff of the disease he had been afflicted, Wade was to pay him 1000 lbs. of tobacco and caske and a Kersey or Broad Cloth Suit, two Shirts and two pair of Stockings, three pair of Shoes and one Barrell of corne or 100 lbs. of tobacco and during Said year was to find him his Dyett & Lodging. We are not told the outcome of this suit.

The other doctors mentioned during this period are Peter Godson, Peter Sharp, Thomas Ward, Emperor Smith, Francis Ottaway, Robert Ellyson, Jacob Lumbrozo, Richard Madokes, John Stansley, John Peerce, Wells, and Waldron. Three of these (Sharp, Godson and Ward) married widows. Of this number Peter Godson impresses us least of all. He was continually in hot water. In 1654 he and his wife are up before the Court for calling Richard Manship's wife a witch.<sup>45</sup> According to the testimony of Bartho: Herring Godson had said to Manship, "Take notice what I Say I came to your house where your wife layd two Straws & the woman in a jesting way Said they say I am a witch if I am a witch they Say I have not power to skip over these Strawes and bid the said Peter Godson to Skip over them and about

<sup>25</sup> Provincial Court, i, pp. 187-188.

<sup>26</sup> Assembly, i, p. 172.

<sup>27</sup> Browne, Hist. of Md., 1884, p. 49.

<sup>28</sup> Council i, p. 119.

<sup>29</sup> Assembly, i, pp. 89 and 116.

<sup>30</sup> Loc. cit.

<sup>31</sup> Assembly, i, p. 167.

<sup>32</sup> Provincial Court, i, p. 231.

<sup>33</sup> Scharf, Hist. of Md., Balto., 1879, p. 237.

<sup>34</sup> Provincial Court, i, p. 239.

<sup>35</sup> Provincial Court, i, p. 158.

<sup>36</sup> Provincial Court, i, p. 264.

<sup>37</sup> Provincial Court, i, pp. 379 and 383.

<sup>38</sup> Provincial Court, ii, p. 96.

<sup>39</sup> Council, i, p. 344.

<sup>40</sup> Provincial Court, ii, pp. 162-163.

<sup>41</sup> Council, i, p. 347.

<sup>42</sup> Provincial Court, ii, p. 491.

<sup>43</sup> Provincial Court, ii, p. 321.

<sup>44</sup> Provincial Court, ii, p. 399.

<sup>45</sup> Provincial Court, ii, p. 87.

a day after the said Peter Godson said he was Lame and thereupon would Maintaine his wife to be a witch." Margaret Herringe's testimony was somewhat similar. She said four straws were laid and Mrs. Manship said to Peter: "In the name of Jesus come over these straws." After mature deliberation the Court ordered Dr. and Mrs. Godson to apologize, acknowledging themselves Sorry for their Speeches and to pay charges. Shortly after this, probably to get even with Herringe, Godson sues him for 1430 pounds of tobacco "for Physick and Surgery impended on his wife." This amount was examined "by men of the same facultie" and was considered exorbitant. It was regulated to 590 pounds which Herringe was ordered to pay in twenty days.<sup>46</sup>

Not many months later Mrs. Godson is up again for slander. This time Michael Baisey's wife is the injured party and Mrs. Godson was "bound in a bond of good behaviour" for two months." Godson himself seems to have discreetly kept his mouth shut on this occasion. In 1655 a most serious charge is proved against him. He is convicted of stealing a bodkin from the wife of John Hamilton and ordered to restore "four fould" and pay the Court charges.<sup>47</sup> Again he is before the Court for not perfecting a cure he promised to perform and for leaving the patient worse than he found him. Godson wisely procured his pay at the onset of the treatment. This the Court ordered him to pay back or perform his undertaking. As he took no notice of this order he is again required to return the stated amount "or Else Execution."<sup>48</sup> The last mention we have of Godson is when Peter Sharp accused him of taking too much blood from Captain John Smith and so causing his death. By the order of the Court the case was "referred to the next Provincial Court when men of Skill and ability shall Judge of the Action." Unfortunately we are not told the result of the suit.<sup>49</sup>

Peter Sharp has left little behind him to tell his tale. After he married Judith Garie he is made administrator of his wife's first husband's estate.<sup>50</sup> His suit against Peter Godson we have previously mentioned. In 1657 he sued Robert Harwood on behalf of his stepdaughter, Elizabeth Gary, for "reparation for slander and unhandsome attempts charged to be acted and reported" by Harwood. It is finally agreed that Elizabeth would go in fifteen days to Thomas Davis' and remain there six weeks. Harwood is to pay for her entertainment there and can court her but must bring one or more neighbors always with him. If at the end of this time she agrees to marry him he is to pay the Court charges, if not Peter Sharp will be liable.<sup>51</sup> Thomas Ward married the widow of Edward Commins<sup>52</sup> of whose estate

he was later appointed administrator.<sup>53</sup> He appears in the Court records as "bringing an unjust troublesome and causeless suit" against two persons, accusing them of unlawful hunting and killing of his hogs. The Court required him to pay to them 500 and 300 pounds of tobacco and caske "in respect of the great trouble and expense they have been put unto in coming from Kent to attend this Court."<sup>54</sup> On another occasion one of these persons, Clay, sues him for slander for defaming his wife.<sup>55</sup> The Court said he had done Clay's wife "a great wrong in the slanderous and abusive words by him uttered concerning her, and to ask her forgiveness for the Same with promise never to wrong her Soe again."

The first item we find about Emperor Smith is that in 1648 he arrested John Nevill about Physick and Chirurgery which he applied to the said Nevill's wife.<sup>56</sup> Nevill denied his treating her. Whereupon Smith got a witness to testify that he was at Nevill's house two years since and heard his wife say "if it had not been for the Dutch Doctor she had not been her own woman." By the consent of both parties the case was postponed till Nevill's wife "returne out of England." Smith elsewhere appears as suing different other people for Physick and Surgery. He is one of the doctors who did an autopsy on Gouge's head, which we will refer to elsewhere.<sup>57</sup>

Francis Ottaway's history is most meagre. Thomas Heben once complains that Ottaway did not bring in "certain medicines this shipping." He then sued him for three pounds sterling. The Court found that as no time was set to Ottaway's procuring these medicines there was no right to grant a process against him.<sup>58</sup> He is again mentioned as suing for some tobacco in roll.<sup>59</sup> Robert Ellyson was a man of some parts. He served on the inquests held upon Anne Thompson, infant,<sup>60</sup> and the Indian lad killed by Dandy<sup>61</sup> and was sheriff of his county<sup>62</sup> for a short time. He appears especially prominent in a suit he brought against Nicholas Hervey for the non-payment of a cure of the latter's servant.<sup>63</sup> Hervey, however, deposed the cure was relinquished before it was perfected by Ellyson and produced Dr. Henry Hooper to sustain this contention. Ellyson, on the contrary, said he did take the cure in hand and did follow it to a good state and was ready to perfect it till he was hindered and put off by Hervey, nevertheless Hervey denieth to satisfie the said price to him. To this statement Hervey said Ellyson did voluntarily neglect and depart from the cure to the endangering of the man's life. Ellyson then claimed the cure was well nighe perfected ere he departed at all from it and if in his absence upon reasonable cause any charge or damage was incurred by Hervey he was willing to deduct it out of his hire as the Court shall think fitt. Though 1200

<sup>46</sup> Provincial Court, ii, pp. 399-400.

<sup>47</sup> Provincial Court, ii, p. 403.

<sup>48</sup> Provincial Court, ii, p. 424.

<sup>49</sup> Provincial Court, ii, pp. 434 and 439.

<sup>50</sup> Provincial Court, ii, p. 432.

<sup>51</sup> Provincial Court, ii, p. 139.

<sup>52</sup> Provincial Court, ii, pp. 531-533.

<sup>53</sup> Provincial Court, ii, p. 228.

<sup>54</sup> Provincial Court, ii, p. 62.

<sup>55</sup> Provincial Court, ii, 233-234.

<sup>56</sup> Provincial Court, ii, p. 235.

<sup>57</sup> Provincial Court, ii, p. 468.

<sup>58</sup> Provincial Court, ii, p. 524.

<sup>59</sup> Provincial Court, i, p. 229-231.

<sup>60</sup> Provincial Court, pp. 256-257.

<sup>61</sup> Provincial Court, p. 221.

<sup>62</sup> Provincial Court, i, p. 139.

<sup>63</sup> Provincial Court, i, p. 260.

<sup>64</sup> Provincial Court, i, p. 231.

pounds of tobacco was demanded the Court found only 800 pounds owing to Ellyson, 400 of which had been paid. He later sued Hervey again for "556 lbs. tob." for attending his wife Jane<sup>63</sup> and is mentioned as bringing two other suits for Physick charges.<sup>64</sup>

Jacob or John Lumbrozo, the "Jew doctor," was established in the Province as early as January 24, 1656.<sup>65</sup> Hollander thinks that he arrived early in that month. He appears to have settled in Charles County and to have enjoyed a lucrative practice. In 1658 he sues David Ferreira for "wages for seven months attendance."<sup>66</sup> A few months prior to this event he was accused of blasphemy,<sup>67</sup> but escaped trial on account of the succession of Richard Cromwell, when a general amnesty was granted to all.<sup>68</sup> In 1663 he is mentioned as "Jacob alias John Lumbrozo, late of Lisbon in the kingdom of Portugal," and was then given letters of denization.<sup>69</sup> By them he was vested "with all the privileges of a native or naturalized subject." Two years later he petitioned for a commission to trade with the Indians and received the same.<sup>70</sup> He died in 1666.<sup>71</sup>

Richard Maddokes,<sup>72</sup> John Stansley<sup>73</sup> and John Peerce<sup>74</sup> are mentioned once, each in connection with performing an autopsy.

Of Mr. Wells, Chirurgion, from St. Mary's County, there is left almost naught but the name. He is paid, in 1639, 20 lbs. sterling out of Mr. Baxter's estate for physick to Mr. Baxter.<sup>75</sup>

Dr. Waldron is mentioned as buying a ring of Francis Brooke's wife and agreeing to give 1000 lbs. tob. for it, which he does not seem to have paid.<sup>76</sup> He was present at the house when the midwife delivered Susanna Warren of a dead child,<sup>77</sup> as will be later mentioned.

Thomas Hebden does not seem to have been a physician. He, however, must have practiced the art of medicine for he appears in the Court records as demanding from the estate of John Cole 50 lbs. tob. for curing Cole's ague & fever about six months afore he went into the flort, 25 lbs. for a purge then likewise, 25 lbs. for stopping of his blood at that time.<sup>78</sup> On another occasion Colonel Francis Traford denied owing him anything or putting "any servant

of his to his physick or board."<sup>79</sup> Hebden sold drugs, we know,<sup>80</sup> and also provided coffins for burial,<sup>81</sup> thus being ready for any emergency. He was a prominent man in the colony and was many times a burgess in the Assembly.

Although there were no woman doctors in those times yet one woman, Katherine Hebden, wife of the above Thomas, seems to have given physick to Richard Lawrence and was paid 1900 lbs. tob. for it, though the sheriff seems to have been backward about giving her compensation till the Court ordered him to do so out of the levy for Physick Charges.<sup>82</sup> In 1643 Thomas Hebden demanded "210 lbs. tob. of Edw. Hall, due for acco<sup>t</sup> of chirurgery of his man's legg & diett per 9 weeks."<sup>83</sup> We later learn that it was Hebden's wife who "did chirurgery upon the legg of John Greenwell, the man-serv<sup>t</sup> of the Said Ed. Hall, & did diett him for 7 weeks, or thereabouts."<sup>84</sup> The Judge found for Hebden the desired amount. An additional item is given about Mrs. Hebden on January 10, 1651, when it is noted that she demanded out of George Manner's estate 140 lbs. tob. & cask for Physick.<sup>85</sup>

As to the price of visits we learn nothing. Tobacco was used in place of money and corn was also employed, on a few occasions, to pay a doctor's bill. Two are mentioned as being paid in pounds sterling. As seen above, Dr. Wade demanded 250 lbs. tob. for two visits paid to Thomas Medwell,<sup>86</sup> but we do not know whether 125 lbs. tob. was the usual price per visit.

Of the drugs used we learn little. In an inventory of an estate in 1639 mithradate and angelica root are mentioned as in the deceased's belongings.<sup>87</sup> The first was invented by King Mithradates and was considered a cure-all. Elsewhere we learn it was a "compound electuary into which entered myrrh, saffron agaric, ginger, cinnamon, frankincense, garlic, mustard, birthwort, galbanum, castor, gum arabic, opium, gentian, valerian, acacia and other substances in Canary wine, honey, etc."<sup>88</sup> It was an alexipharmic or a medicine proper for expelling morbid principles or preventing bad effects of poisons taken inwardly.<sup>89</sup> Angelica root was an aromatic and carminative. Sweet meat was made from it.

The delusion of witchcraft found little soil to grow or flourish on in Maryland. There was one execution for it and this was in 1684.<sup>90</sup> We will speak of it in a subsequent paper. In 1654 Mary Lee was executed as a witch on high seas, in a ship bound for the Province. The records relate something concerning it.<sup>91</sup>

Midwives during this period alone practiced obstetrics. I have been able to find the names of three of them. In

<sup>63</sup> Provincial Court, i, p. 294.

<sup>64</sup> Provincial Court, i, pp. 267 and 301.

<sup>65</sup> Hollander, Some Unpublished Material Relating to Dr. Jacob Lumbrozo of Maryland. Pub. of the Am. Jewish Hist. Soc., Balto., 1893, i, pp. 25-39 and Civil Status of the Jews in Maryland, 1634-1776. Pub. of the Am. Jewish Hist. Soc., Balto., 1894, ii, pp. 38-40.

<sup>66</sup> Provincial Court, iii, (MS.), folio 136.

<sup>67</sup> Provincial Court, iii, (MS.), folio 159-160.

<sup>68</sup> Provincial Court, iii, (MS.), folio 215.

<sup>69</sup> Council, i, p. 488.

<sup>70</sup> Council, ii, p. 65.

<sup>71</sup> Council, i, p. 526.

<sup>72</sup> Provincial Court, i, p. 104.

<sup>73</sup> Hollander, Op. cit.

<sup>74</sup> Provincial Court, ii, p. 136.

<sup>75</sup> Loc. cit.

<sup>76</sup> Provincial Court, ii, p. 171.

<sup>77</sup> Provincial Court, ii, p. 97. The first reference to malaria I can find in the Province. Hebden nowhere appears in the Records as a "physician or chirurgion." He is frequently styled planter. His wife Katherine seems to have been somewhat skilled in chirurgery, as we see later.

<sup>78</sup> Provincial Court, i, p. 197.

<sup>79</sup> Provincial Court, ii, p. 400 and elsewhere.

<sup>80</sup> Provincial Court, i, p. 107.

<sup>81</sup> Provincial Court, ii, p. 123.

<sup>82</sup> Provincial Court, ii, p. 415.

<sup>83</sup> Loc. cit.

<sup>84</sup> Provincial Court, i, p. 244.

<sup>85</sup> Provincial Court, i, p. 77.

<sup>86</sup> Provincial Court, i, p. 268.

<sup>87</sup> Dunglison's Medical Dictionary.

<sup>88</sup> Dunglison's Medical Dictionary.

<sup>89</sup> Scharf, Hist. of Md., Balto., i, p. 297.

<sup>90</sup> Council, i, pp. 306-308.

August, 1651, Mary Clocker delivered Susannah Warren of a dead child which had no imperfection. "Likewise with hair up on its head & nails upon its fingers and toes." Dr. Waldron, who happened to be in the house at the time, said the mother "had gone out her full terme and that the Child had been dead as he did Suppose three weeks in its Mother's womb." Mrs. Clocker further relates that "the child was free from boyles or botches, or any disease, Saving only that a little of the Skinn was broken to the bredth of betwixt two or 3 fingers and about 4 inches long coming from under the arm upon the Stomach which she doth Suppose it [due to] being Soe long in her Womb."<sup>93</sup> A little later Mrs. Johnson<sup>94</sup> is mentioned as a midwife on another occasion and still later Rose Smith "received into the world a man child about three months old." "It was all bruised one side of it." The abortion was due, according to the woman's testimony, to her husband beating her with a pair of "tongues."<sup>95</sup>

Juries of women are now and then noted as being required to report on the condition of one of their sex. We give two instances. In 1656 eleven women are impaneled to search the body of Judith Catchpole, who was suspected of murdering her child while on the ship *Mary and Francis*, bound for the Province. Her accuser was deceased. He swore the act was done when "all the people & the seamen were asleep." The women reported that according to their best judgment she "hath not had any child within the time charged." She was accordingly acquitted by the Court, who said at the same time that the party accusing seemed not to be in a sound mind.<sup>96</sup> In the next year another jury of women searched Elizabeth Robins and found her with child.<sup>97</sup>

Inquests were held early and the causes of death were diligently searched into. One of the first items in the first volume of the proceedings of the Provincial Court is an account of the inquest of twelve planters, held January 31, 1637, on John Bryant, killed by the fall of a tree at Mattapient. They report that by the said tree his "bloud bulke" was broken and that "the said tree moved to the death of the said John Bryant; & therefore they find the said tree forfeited to the Lord Proprietor."<sup>98</sup> On March 23 and 24 of the same year inquests were made on the bodies of two men "drowned by misadventure."<sup>99</sup> Five years later twelve men, on November 5, hold an inquest before the Sheriff upon the view of the body of Anne Thompson, infant. They report "that they doe not find anything but that the said Anne came to a natural death."<sup>100</sup> A few months after this

Edward Packer as Sheriff and Coroner is asked to "take & impanell as many freemen as conveniently he may to enquire by what meanes a certaine Indian ladd (since called Edward) came by his death, and to administer an oath to them & evidence retorn without delay." A jury of twelve men gave the following return of the inquest on Feb. 23, 1643.

"We find that this Indian (named Edward) came by his his death by a bullett shot by John dandy, which bullett entered the epigastrium near the navell on the right side, obliquely descending & piercing the gutts, glancing on the last vertebra of the back, and was lodged in the side of Ano."

foreman

George Binx.

This jury then filed the following report that Dandy assaulted the Indian "and one gonne charged with bullets against the said Edward did discharge, & therewith did wound the Said Edward in the right side of his belly neare the navell, so that he pierced his gutts, of which wound the said Edward afterwards within the space of 3 daies died."<sup>101</sup> Dandy plead not guilty to this charge and was then tried by a jury of twelve men who brought in a verdict of guilty of "felony and murder."

He was a blacksmith by trade and so "too valuable a member of the community to be lightly parted with."<sup>102</sup> "Upon the petition of the great part of the colony for the pardoning of Dandy," his sentence was exchanged to "three years service to the Lord Proprietary."<sup>103</sup> He was adjudged "publique executioner within the province,"<sup>104</sup> that is, public flogger and hangman. This office frequently seems to have gone a-begging. On another occasion the death sentence on a man was commuted if he would be a common hangman.<sup>105</sup>

In 1647 Governor Greene acquitted Dandy "from all such penalties and censures."<sup>106</sup> As Dr. Browne says,<sup>107</sup> it would have been economy to have hanged him, for in 1657 the Court, thinking Henry Gouge to be brought to an untimely end by his master John Dandy, ordered "Mr. James Veitch to go where the said Gouge is interred and to Cali So many of the neighbors as Conveniently can be procured with two Chirurgeons viz: Mr. Richard Maddokes and Mr. Emperor Smith." After a "diligent view is taken of the Said Corps the Said Chirurgeons in the View of those that Shall be then present, are to take the head of the Said Corps and after diligent View and Search to Signifie under their hands, how they find the Said head & Corps, and are to cause the Said head to be Carefully lapped up and warily brought to the Court with what convenient and possible

<sup>93</sup> Loc. cit.

<sup>94</sup> Provincial Court, II, p. 285.

<sup>95</sup> Provincial Court, II, pp. 464-465.

<sup>96</sup> Provincial Court, II, pp. 456-458, and Quinan's article, op. cit., pp. 180-181.

<sup>97</sup> Provincial Court, II, p. 555.

<sup>98</sup> Provincial Court, I, pp. 9-10.

<sup>99</sup> Provincial Court, I, p. 24.

<sup>100</sup> Provincial Court, I, p. 139, and Quinan's article, op. cit., pp. 275-276.

<sup>101</sup> Provincial Court, I, pp. 254-255 and 260, and Quinan's article, op. cit., p. 276.

<sup>102</sup> Browne, Hist. of Md., 1884 p. 53.

<sup>103</sup> Council, I, p. 98.

<sup>104</sup> Council, I, pp. 187-188.

<sup>105</sup> Council, II, p. 499.

<sup>106</sup> Council, I, p. 187.

<sup>107</sup> Browne, Loc. cit.

speed as may be."<sup>108</sup> Eleven men formed this inquest. They report they "diligently viewed the head of the Corps of Henry Gouge. And being laid open to us by the Chirurgeons which was Ordered by the Court to View and Lay it open unto us. We here detest under our hands that we can See nor find nothing about the Said head, but only two places of the Skin and flesh broke on the right Side of the head and the Scull perfect and sound, and not any thing doth or can appear to us to be any cause of the Death of the said Gouge. And alsoe we doe detest that we did Endeavor what possible in us lay to Search the body of the Said Corps and could not possibly do it; It being so noysome to us all, and being put at first into the ground without anything about it, as the Chirurgeons and the Sheriffe can satisfie you."<sup>109</sup> Dandy was subsequently brought to trial and, upon the testimony then given, was condemned to death. He escaped to Virginia, but was apprehended, brought back and finally executed.

Maddokes and Smith do not seem to have been paid for this autopsy, so that they finally petitioned the Court for "Satisfaction for their trouble and paines in viewing the Body of Henry Gouge late murdered, and desecting the head from the said Corps." They were accordingly allowed one hoghead of tobacco to be equally divided between them.<sup>110</sup>

In 1648 George Manners is "ordered to impannell a jury of 12 men to make inquiry of the death of Tho: Allen fowned dead upon the sands of Poynt Lookoe out in St. Michael manor." On the next day through their foreman, Edward Cottam, they report that they found "Thomas Allen was shott under the right shoulder, & hath three holes but whether with shott or Arrows they know not. His Corps is so eat & consumed. And likewise that a great peice of his skull is broken & taken away; & the skin of his scull is broken & taken away; and the skin of his scull is flayed of quite round his head."<sup>111</sup> On the back of Allen's will was found this remarkable statement: "I desyre that & if I should sodenly dye, & the cause how, should not be directly knowne how, or where, or when. That there bee speedy Enquiry made, how & where and what was the cause. And if it be not directly fownd then I would have Nick: & Marks att Pyney-neck, Irish men, questioned as suspitious persons: for reasons to mee best knowne. This more I desyre of you my freinds John Hatch, & Richard Banks & soe likewise of you my Sonnes Thomas, William, & Robert Allen. This is my desyre. Wittness my hand this twenty-

third of Aprill Ano Dni 1648."<sup>112</sup> We learn nothing of the subsequent history of the affair.

A few years later Ralph Beane was suspected of foul play to his servant Ralph Loe. At the investigation a man named Simpson makes deposition that he with Mr. Budd found Loe gro[veling on the] Timber and rattling in the Throate and not knoweing conveniently h[ow to carry him] off, thay willed Ralph Beane to fetch a Chayre weh hee did, and p[ut]ting him there the[re] man still remayned rattling in the throate and drab[ling at the mou]th. And as they[re] were carrying him to the House, the Said Man fetched a great groane, an[d dyed in the Chaire]. Simpson further says "hee sawe noe blood abo[ut him or any] blowe or harme or any outward appearance occasioning his death but [that he verily] believeth that hee dyed of some imposthume or apoplexy." A jury of twelve men, after due consideration, decided that Beane was in no way accessible to his death, "but in regard hee gave occasion of the Charge ensuing thereupon by his private and Suddayne buriall of him dyeing suddenly It is ordered that hee the said Ralph Beane shall satisfie the same, being as followeth viz: to the Chirurgeons, Widowe or Administratrix nowe the wife of Thomas Bushell One thousand pounds of tobacco and Caske. To the Sheriffe for his Coroners flee two hundred pounds of Tob: and Caske and for impanelling the Jury & Sumoning Witness three hundred pounds of Tob: & Caske, And all Court Charges."<sup>113</sup>

On July 20, 1670, John Stanley and John Pearce, Chirurgeons, are ordered to view the head of Benj. Price and "certify what their opinions are touching the death of the said Price."<sup>114</sup> He was thought to have been killed by the Indians.

The first act for the regulation of Coroner's fees was passed by the Assembly in 1671. The amount was fixed at two hundred and fifty pounds of tobacco "for their viewing the bodies of any pson or psons murdered Slayne drowned or otherwise dead by Misadventure." It was to be "paid and allowed to them out of the goods or Chatles of the Person Murthered or Slayne (if they had any)."<sup>115</sup> If not, the amount was to be obtained by a County Levy.

From the above sketch we may conclude that Maryland has no reason to complain of her early doctors. Some, it is true, were too free with the use of their tongues, as the records well show, and others, as Peter Godson, savor somewhat of the charlatan. Yet all in all they were a set of men abreast with their times. They seem to have served well their day and generation.

<sup>108</sup> Provincial Court, ii, pp. 524-525, and Quinan's article, op. cit., pp. 51-52.

<sup>109</sup> Provincial Court, ii, p. 525.

<sup>110</sup> Provincial Court, ii, p. 546.

<sup>111</sup> Provincial Court, i, p. 403.

<sup>112</sup> Provincial Court, i, p. 404.

<sup>113</sup> Provincial Court, ii, pp. 73-74.

<sup>114</sup> Council, ii, p. 65, and Quinan's article, op. cit., p. 51.

<sup>115</sup> Assembly, ii, pp. 293-294.

## THE JOHNS HOPKINS HOSPITAL BULLETIN.

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Volume XII is now completed. The subscription price is \$1.00 per year. The set of twelve volumes will be sold for \$30.00.

SOME DISTINGUISHED AMERICAN STUDENTS OF TUBERCULOSIS.<sup>1</sup>

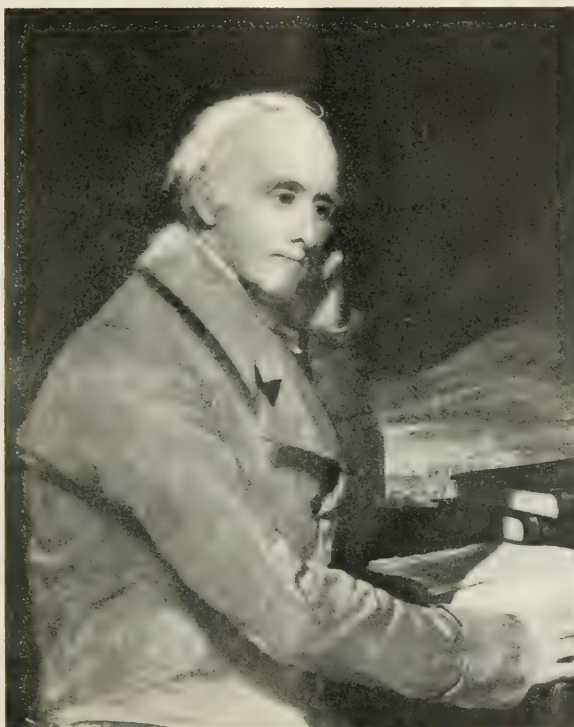
BY HENRY BARTON JACOBS, M. D.,

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In considering this subject I shall deal with the past rather than with the present, and as we stand here on the illumined heights of the twentieth century and cast our eyes downward and backward over the history of tuber-

gative students in any branch of medicine are not to be found.

Rising out of this gray obscurity, on the very horizon of our vision, elevated by some irresistible internal force,



DR. BENJAMIN RUSH.

From painting by Sully.

culosis in our country, several figures, conspicuous above their fellows, stand forth as beacon lights along the way. In the far distance, view is lost in the mists of the early centuries of American practice, when physicians toiled for their patient's good in paths laid down for them by the old European masters, without time, inclination, or facilities, for questioning these guiding principles, and real, investi-

avored by new conditions, new surroundings, the establishment of a general hospital, the beginning of clinical teaching, the face of the first true student appears, Benjamin Rush, the Sydenham of the new world.

Born in 1745, near Philadelphia, receiving his early education from Reverend Samuel Findley in Nottingham, Maryland, "among a people remarkable for their simplicity, industry, morality and religion," young Rush went to Princeton in 1759 and after obtaining the degree of Bache-

<sup>1</sup>Read before the Laennec Society of the Johns Hopkins Hospital, February 26, 1902.

lor of Arts in 1760 when yet under fifteen years of age, at once entered the office of Dr. John Redman of Philadelphia as a student of medicine. The books of Hippocrates were given him to read and these he transcribed from Greek into English. In 1766 when Cullen was at the height of fame Rush proceeded to Edinburgh, graduating there two years later. Some time was then spent in London and Paris, but in the fall of 1769 he returned to Philadelphia to begin the practice of physic. At once he was elected professor of chemistry in the college of Philadelphia, making the fifth of the group of men, Drs. Shippen, Morgan, Kuhn, and Bond which composed the faculty of this first medical school of America. Here for forty-four years he remained a teacher of medicine, two successive generations of pupils, fully 2250 in number, receiving their inspiration from him. From the time he began his diary when seventeen years old he never ceased to write to the day of his death. Not one subject alone but all subjects connected in the remotest degree with medicine received attention—whatever pertained to good living, good citizenship, or the advancement of the city and country was of interest to him. His style was original, forceful, concise, his observations careful and his conclusions logical. When he returned to Philadelphia medicine was being practiced under the Boerhaavian system, which located disease in the fluids of the body. This method soon yielded to the newer teachings of Cullen. Rush dissatisfied with this turned to the older methods of Sydenham and determined to study disease from the view-point of its natural history. He taught that the name of a disease means nothing, that its nature is everything, "that with observation must be combined a perfect knowledge of all the causes of disease, a knowledge to be completed by the labours of physicians in generations or perhaps ages to come." The influence of Rush upon American medicine through his long life can scarcely be estimated, for his many publications founded upon his wide practical experience went with his pupils into the most distant parts of the country. Time does not permit consideration at any length of his writings beyond those devoted to tuberculosis. In him we find our first distinguished student of that disease. In his "Thoughts upon the Causes and Cure of Pulmonary Consumption," published in 1783 he says, "The ancient Jews used to remark that a man does not fulfill his duties in life who passes through it without building a house, planting a tree and leaving a child behind him." "The physician in like manner should consider his obligations to his profession and to society as undischarged who has not attempted to lessen the number of incurable diseases. This is my apology for presuming to make consumption an object of medical inquiry." This paper was followed by a second with a similar title, which is practically an elaboration of the first. Several points in these may be interesting to bring to your attention. The first proposition states that pulmonary consumption is a disease of debility; the second, that pulmonary consumption is primarily a disease of the whole system and debilitating causes tend to produce it; the third,

that cough, ulceration and purulent or bloody discharges from the lungs are the *effects*, not the *causes* of the disease. Dr. Rush asserts that consumption is unknown among the Indians of North America, although this view has been controverted by Barton, that it is scarcely known to those citizens of the United States who live in the first stage of civilized life, i. e., the first settlers. The principal occupation of the Indians consisted in war, fishing and hunting, that of the first settlers in fishing, hunting, and the laborious employments of subduing the earth, cultivating the fields. The disease is less common in country places than in cities, among those whose business requires them to live in the open air at all seasons of the year, than among men who work under cover. Hence the cure for consumption is to revive the manner of living of the Indian and the first settler, to resort to exercise or labor in the open air. With scorn he sets aside such medicines as syrups and decoctions, for not one of them all without the aid of exercise has cured a single case of consumption. Tubercles are the consequence and not the cause of the disease. Tubercles are the effects of general debility communicated to the bronchial vessels causing them to secrete a supernatural quantity of mucus. Many distinguished physicians have agreed that consumption is dependent upon contagion. In this opinion early in life he acquiesced, but later was led to call its truth in question.

His treatment of consumption, as of most diseases, depended upon the state of the patient's system; if in the plethoric state, i. e., with high bounding pulse and fever, then depletion was demanded by frequent bleeding, low diet and purges; if in the debilitated state, i. e., with weak small pulse with or without night sweats and hæmoptysis, then a sustaining treatment was indicated—full diet, alcohol, tonics. In either condition the *radical treatment* consisted of exercise in the open air, graduated so as to induce fatigue, active exercise if possible, passive, if necessary.

In the question of food and air and exercise it is remarkable how exactly his ideas coincide with ours to-day a full hundred years later. Two other papers bearing upon consumption, the first "On the Climate of Pennsylvania"—the first climatological essay in America based upon careful observations, and the second "An account of the efficacy of common salt in the cure of Hæmoptysis," appeared from his pen.

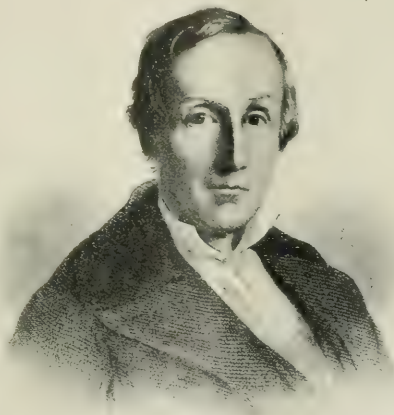
As regards the character and attainments of Dr. Rush let me quote a few desultory words from Professor Francis: "It is no easy task to do justice to his great talents, his vast labors and his exemplary character; his kindness and liberality was unbounded; his mind was of a superior order, possessing a discriminating judgment, a retentive memory, a brilliant imagination, a highly cultivated taste. An incessant and unwearied student, at the head of medical practice in a large and populous city, the first of medical teachers in a great university, a most assiduous prescriber for its extensive hospitals, moreover, among the most voluminous

and able writers of the time. His habits of punctuality the subject of general encomium; as physician to the Pennsylvania Hospital he was never known to vary ten minutes in his professional appointments from the hour of attendance during the long period of thirty years. No mere collator of the opinions of others he was constantly making discoveries, established more principles and added more facts to the science of medicine than all who had preceded him in America."

his greatness as they may to that of any who will follow them: "Medicine is my wife, science is my mistress, books are my companions, my study is my grave, there I lie buried, the world forgetting, by the world forgot."

The next name worthy to follow that of Benjamin Rush is that of Samuel George Morton, "a name which at once adds lustre to American medicine and to American learning."

Born in Philadelphia in January, 1799, he received his early education under strict Quaker influences and soon



SAMUEL GEORGE MORTON.

As a citizen he was ever active lending his voice and his pen to all that looked to the public good, a strong advocate of republican democracy he signed the Declaration of Independence and supported the Revolution in every possible way.

His writings perhaps of greatest value aside from his volume on Diseases of the Mind are his papers upon Consumption and his general histories of the Epidemics of the United States, particularly yellow fever.

He died April 19, 1813, after only five days' illness, probably of pneumonia, when 68 years old.

In the early years of his life he took the words which follow for his motto; words which perhaps contributed to

was put to work in a mercantile counting room. The life, however, was distasteful and he determined to study medicine, so when eighteen years old he entered the office of Dr. Joseph Parrish, at the same time attending courses of medical lectures in the University of Pennsylvania. Among Dr. Parrish's assistants was Dr. Richard Harlan who was interested particularly in the study of natural history, especially zoology. With him young Morton formed a fast friendship and by him was early taken to meetings of the Academy of Science and doubtless from him first received that inspiration for the study of nature and her works which became the passion of his life.

In 1820 at the age of twenty-one he received his degree

of doctor of medicine and was immediately elected a member of the Academy of Science.

Being asked now by an affluent uncle living in Ireland to visit him he set out at once and was warmly received by this relative, who soon became so attached and proud of his young nephew that he determined to give him the advantage of a degree from Edinburgh. His diploma from the American university not being considered as admitting him to advanced standing, he found it necessary to enter for the full course, so he spent much time in cultivating the classics, in acquiring the modern languages and in studying geology. The winter of 1821 was passed in Paris, and he speaks of it in his diary as the happiest thus far of his life. He followed the clinics of Laennec and in the preface of his book on Consumption says, "My attention was first particularly directed to the diseases of the lungs by an attendance on the clinical lectures of the celebrated Laennec; who, with astonishing acuteness of mind, and personal urbanity, combined the faculty of imparting a portion of his enthusiasm to all who heard him."<sup>2</sup>

Going back to Edinburgh he received the degree of M. D. in 1823. Always fond of books, of a poetical temperament, affectionate disposition and a magnetic power of attracting men to him, these years in Europe, Europe so full of all that appeals to the gentle and aesthetic side of man both in literature and in art, these I say, were years of inconceivable delight and happiness to this gentle, intelligent, poetical young man, but they did not weaken his enthusiasm and purposes. Returning to Philadelphia in 1824 he immediately began to practice medicine and became one of the very first in America to introduce the physical means of diagnosis in thoracic affections which he had learned in Paris. He seems also to have resumed at once his labors in the Academy of Science, his first papers read in 1827 being devoted to geological topics.

In 1834, when 35 years old, his volume on Pulmonary Consumption appeared, and in this he must be considered one of the earliest investigators of the morbid anatomy of that disease—indeed actually the first in this country. "It will always stand as a monument of his industry and accuracy and a credit to American medicine." He says in the preface, "On my return to my native city I resolved to pursue with ardour an inquiry for which I had imbibed from Laennec so strong an interest. But facilities are not always at our command. At length in 1829 I received the appointment of physician to the Philadelphia Alms House Hospital. The wards of this institution habitually containing several hundred patients, many of whom are afflicted with phthisis, while the facilities for pathological investigation are unrivalled on the American Continent." So it is that he made the book from his own experiences—comparing constantly the history and symptoms with the findings after death.

He also constantly compares the results of his observations with those of the French pathologists, agreeing with them for the most part but not hesitating to take exception to their views if his investigations do not coincide. The volume is particularly noteworthy for the beauty and accuracy of its plates drawn from life and colored at once under his own supervision. Indeed these are among the first colored medical plates found in this country.

A phase of the subject to which he devoted much thought and observation was the nature of tubercles, that phase which was the stumbling block to all students of the disease, finally he summed up with these words:

"1. Tubercles are an altered secretion of the albuminous halitus proper to the cellular tissue forming the parenchyma of organs.

"2. Inflammation is not necessary to their development.

"3. The cellular tissue which envelopes and intersects tubercles, sooner or later takes on inflammation, and secretes pus; by which process the tubercular matter is eliminated, and an abscess is formed."

It is remarkable how accurate these conclusions are; there is little wanting except an explanation of the primary cause of the altered secretion.

In speaking of the cause of consumption he does not hesitate to boldly consider bronchitis as a frequent contributing factor, in this widely differing from Laennec. In substantiation he refers to the frequency of pulmonary tuberculosis in those who work in flax mills, or inhale dust or mineral spiculae in the iron trades. Surely this is an observation which later investigation fully confirms.

This book met with such well merited approval that Dr. Morton felt justified some years later in issuing a second edition in which he embodied his increased experience, thus enlarging the volume from about 180 to 340 pages. More attention was paid to the therapeutics of the disease, particular stress being laid upon the efficacy of open air life and exercise.

In regard to the essential nature of consumption, however, later experience added no new light and the first edition stands as the real result of his genius.

In 1839, when forty, he published a text-book on anatomy, a volume which for many years was used in the schools of the country. It had colored plate illustrations which proved of inestimable service to students in regions where anatomical material was scarce.

This same year appeared the first of his volumes from his collection of crania, *Crania Americana*, followed in 1844 by *Crania Aegyptica*. It is upon these works that his international fame is chiefly dependent. Having occasion to deliver an anatomical lecture in 1830 upon the difference of the *Crania* of the Five Races of Men he was astonished to find that it was utterly impossible to obtain two skulls—those of the Malay and Mongolian—for illustration. He determined to supply the deficiency and thereupon set about making a collection. This finally became a passion for him and he had men in all parts of the world looking for crania

<sup>2</sup>This is the only personal reference to Laennec I find in any American writings.

of various epochs and races. Nor was he a mere collector but a student as well, and so his writings upon them became not only ethnological but philosophical. The conclusion was inevitable that if the same difference now seen existed in the skulls of different races 3000 years ago it could not be possible that these differences had occurred in the preceding 1000 years to the time of Adam, hence Adam could not be the first man. At the time of his death his museum of crania numbered 1656 skulls and represented the expenditures of many thousands of dollars and of much time in gathering them together. With all this work he edited four editions of Mackintosh's System of Medicine, wrote numerous papers and attended to his hospital and a large private practice.

He died May 18, 1851, two days after a stroke of apoplexy accompanied with hemiplegia in the fifty-second year of his age—a truly lovable man, of delicate instincts, refined intelligence full of cordiality, whose house was the resort of all learned men of his day—poetical in his tastes, and fond of writing verses, diffident, yet courageous and strong in his convictions, devout yet ready to follow the truth wherever it might lead.

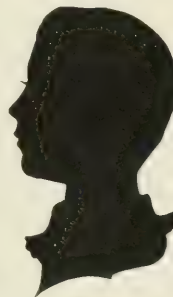
I cannot forbear quoting one stanza of his poem written on the occasion of a visit to Kilcoleman Castle, County Cork, Ireland, where Spenser lived and is believed to have written his immortal poem.

The flocks are fled, and in the enchanted hall  
No voice replies to voice; but there ye see  
The ivy clasp the sad and mould'ring wall,  
As if to twine a votive wreath for thee:  
All—all is desolate—and if there be  
A lonely sound, it is the raven's cry!  
Let years roll on, let wasting ages flee,  
Let earthly things delight, and hasten by,  
But thy immortal name and song shall never die!

I now wish to call your attention to a group of ardent young men, who following some years later in the footsteps of Morton, were attracted to Paris by the brilliant teachings of Laennec and his colleagues and successors, Bayle, Louis, Chomel, Andral. The first of these to whom I shall refer is James Jackson, Jr. No history of American students of Tuberculosis would be complete which omitted mention of his inspiring life and work. Though it was short, yet in those few years there was accomplished much and an example set for all students to follow.

Born on the 15th of January, 1810, Jackson graduated at eighteen from Harvard College and immediately began the study of medicine as a pupil of his father, attending also medical lectures in the Harvard school and at the Massachusetts General Hospital. In 1831, when Louis full of fame for his study of disease according to the numerical method and Laennec's means of diagnosis were proving of such assistance to the student of pulmonary disease, young Jackson visited Paris and soon became the favorite pupil and warm friend of Louis and gave evidence of being a truly

worthy disciple of that master. So fond of him indeed was Louis and such a believer in the young student's character and ability that he endeavored to persuade him to remain with him as an assistant. But his father advised against it. Returning home to Boston he received the degree of Doctor of Medicine from Harvard in 1834 and immediately entered into active practice. Sadly enough, however, this career was shortly cut off by his untimely death from typhoid fever on the 27th of March when but in his twenty-fifth year. In Paris young Jackson kept accurate notes of the cases seen, studied them carefully, learned the use of the new methods of procedure in physical diagnosis, became an adept with the stethoscope and by his enthusiastic letters in regard to its usefulness stimulated those at home to give it trial. In this memoir which I show you published by his father there are gathered together many of these letters, also with his notes and commentations.



JAMES JACKSON, JR.

This is the only likeness in existence made when eight years old, kindly loaned by Dr. James Jackson Putnam of Boston.

thirty of the cases which he studied. While it is not possible to say that young Jackson made any material contribution to the knowledge of tuberculosis it must be remarked that he added a wonderful stimulus to its study and that he was the first to suggest one of the earliest stethoscopic physical signs of that disease, a sign which Louis and all authors since have accepted, one that we now teach as among the very first signs of the disease, namely, the prolongation of expiration over the part infiltrated with tubercles.

I scarcely know any book which is more of an inspiration to the medical student, more of an incentive to hard work and to high ideals than the little story of the life of this young man.

The second of the group is William W. Gerhard, who was born in Philadelphia, July 23, 1809.

In 1823 he entered Dickinson College and graduated in 1826 at the age of seventeen. Returning to Philadelphia he was taken into the office of Dr. Joseph Parrish as his

pupil in medicine, following at the same time the courses in the University of Pennsylvania from which he received his degree of Doctor of Medicine in 1832. Immediately afterward he set out for Paris and there devoted himself particularly to the teachings of Louis, observing disease and collecting materials with which he might himself benefit science.

While still in Paris he made his first publication in conjunction with Caspar W. Pennock on Asiatic Cholera as it appeared in that city in 1832. After this he became interested in studying children's diseases and so confined him-

a careful study he was able to announce that it was no mere modification of the autumnal typhoid but rather a new disease identical with what he had seen in Edinburgh and utterly distinct from the typhoid of Paris and Philadelphia. In 1836 he became one of the editors of the Medical Magazine, and a clinical lecturer in the Philadelphia Hospital. No man in his day enjoyed such a high reputation as a lecturer.

It is particularly the volume published in 1842 to which I wish to call your attention, a work on Diagnosis, Pathology and Treatment of Diseases of the Chest, a work which



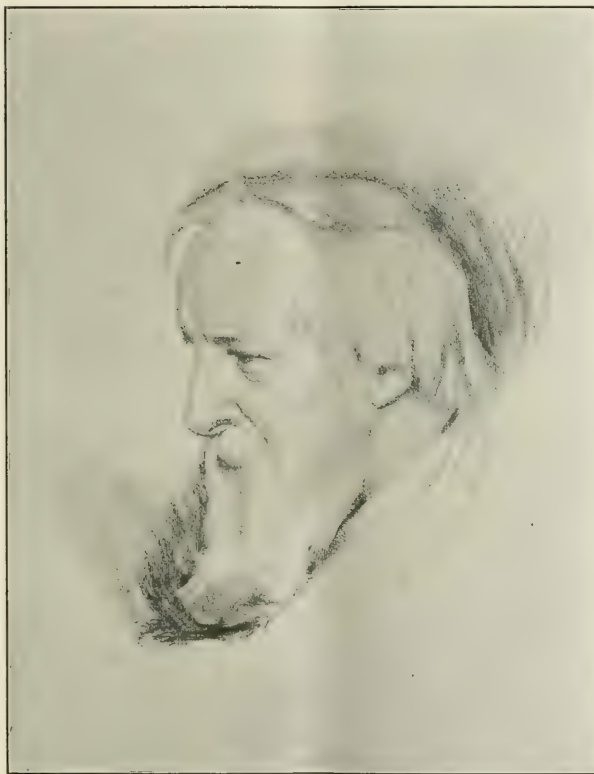
WILLIAM W. GERHARD.

self almost exclusively to the Hospital of Sick Children, where as a result of his observations and analyses of cases he succeeded in associating that most common form of meningitis of children with a deposit of tuberculous material in the pia mater. This seems to be the first recognition of tuberculous meningitis. In 1833 returning home he became resident physician of the Pennsylvania Hospital. After observing a series of cases of our autumnal fever he was able to establish its identity with that prevailing in Paris both in symptoms and anatomical characteristics. But he was not slow in lending his aid to the study of diseases of the chest, a small octavo volume on this subject appearing in 1836. His object in this was mainly to facilitate a knowledge of the physical signs which practitioners in this country were so tardy in learning. In this year, 1836, Philadelphia was visited with an epidemic of typhus fever and after

reached a fourth edition in 1860, increasing in size from 157 to 448 pages, devoted to an exhaustive consideration of the subject as known in this country and in Europe and perhaps more useful in disseminating a knowledge of the disease throughout the country than any that had yet appeared. Gerhard displayed little of originality in the book, but by bringing together all that was known of the disease he did his fellow practitioners an inestimable service and so stimulated a study of pulmonary complaints and brought about a much more rational method of treatment. His skill in pulmonary diseases came to be so well recognized that he was called to all parts of the country in consultation and by his personal example and continual teaching spread a further knowledge of these affections and the proper physical signs pointing to their diagnosis. He died of apoplexy, much beloved and very highly respected, April 28, 1872, aged 63 years.

The third member of that brilliant band of young Americans who went to Paris for inspiration and knowledge and who returned full of enthusiasm for prosecuting the work is one whose name will long stand upon the roll of the most distinguished students of tuberculosis in this country—Henry Ingersoll Bowditch. I may be permitted to mention that the biography of him which will soon be published will

sympathetic, truthful, manly; in college the same warm-hearted, good fellow, straightforward, ardent, sensitive and popular. He graduated from Harvard in 1828, from the Medical School in 1832 and at once received the appointment of house officer in the Massachusetts General Hospital, then spent two years in Europe studying with Andral, Chomel and particularly Louis. He was a member of that



HENRY INGERSOLL BOWDITCH.

From a charcoal drawing kindly loaned by his son, Dr. Vincent Y. Bowditch, of Boston.

contain an account of the life and works of one of our very noblest of American physicians—one who exerted a greater influence upon the profession in New England and upon the affairs of the city and state in which he lived than any other medical man of his time. As a student of tuberculosis he left an impression that must always be considered in any review of the progress of our knowledge of that disease. Briefly only will I refer to his career. He was born in Boston in 1808, the son of Nathaniel Bowditch, an eminent mathematician. As a school boy he was kind, generous,

brilliant Society of Observation in Paris and became the life-long friend of its president, Louis. On returning to Boston he took up the study and practice of medicine with full enthusiasm for the methods learned in Paris. From 1838 to 1845 he filled the position of admitting physician to the Massachusetts General Hospital; from 1846 to 1864 served as visiting physician to that hospital and from 1878 to 1881 visiting physician to the City Hospital; while from 1859 to 1867 he held the chair of professor of Clinical Medicine in the Harvard school. An incident connected with his

appointment as admitting physician to the Massachusetts General Hospital is a typical illustration of his character and exemplifies his universal love for all sorts and conditions of men. At that time negroes were not received as patients in the hospital. A negro with pneumonia presented himself, was accepted by Bowditch but was refused admittance by the superintendent. Immediately Dr. Bowditch resigned his position, which the trustees finally decided not to accept, so ever afterwards there was no distinction made with regard to the color of patients. To his professional associates he was always an inspiration. To the younger men his unflinching kindness of heart and generosity gave strength and courage. He became a great leader in sanitary science and before a committee of the state legislature advocated its necessity with such power that he did much to persuade it to create the first State Board of Health in this country. Of this he became the first president in 1869, a position which he held at a great sacrifice of his time for professional work. He also was one of the first to believe in women physicians and advocated successfully their admittance to the Massachusetts Medical Society when competently educated.

His impress upon the subject of tuberculosis in this country is found first in bringing back to Boston the enthusiasm which he had received from his masters in Paris and in his efforts to induce his fellow practitioners here to follow their example. To farther these efforts he gathered about him a number of the younger and more progressive men to form a society for medical observation upon the same lines as those of the Observation Society in Paris. His next effort was to scatter the knowledge of the use of the stethoscope and its principles and to this end he published a small book called "The Young Stethoscopist or the Student's Aid to Auscultation," which went through two editions. Next he edited for the benefit of American readers Louis' Treatise upon Phthisis. Being struck with the fact that consumption was unequally distributed in New England he attempted an inquiry to determine the reason and embodied his research in a communication to the Massachusetts Medical Society entitled "Consumption in New England or Locality one of its Causes," published in 1862. By this inquiry he was led to believe that soil moisture was a productive agent in causing the disease. Later in a second edition in 1868 he was able to substantiate this doctrine by statistics from old England as well as New England which indicated a diminution in the disease after proper artificial drainage or the removal of families to more elevated and dryer spots. In 1864 he was the first to advocate strongly that which for the preceding years of the century had been overlooked, or for the most part not conceded, namely, that in certain instances consumption was contagious or at least infectious, and therefore to him must be given the credit of reviving the doctrine of the early writers, a fact which the researches of Villemin a few years later so fully confirmed.

Nor must be omitted mention of that which will always give to his name its greatest prominence, namely, his insist-

ent and constant practice of thoracentesis. In the year 1850 having a patient with a pleuritic effusion, against the advice of his fellow practitioners, he made use of Dr. Wyman's trocar and aspiration bottle for withdrawing the fluid from the chest. Success attended his efforts and from this time on for many years he was a constant and almost the sole advocate of this procedure. Undaunted, however, by much opposition he continued its use and in 1855 was able to report 25 cases in which the operation had been successfully performed. Some years later this number had grown to nearly 308 and the results in all were so striking that the conclusions he reached were irresistible, and thus practically through his sole efforts the operation of tapping the chest came to be universally employed. He died full of years and honors January 14, 1892, when 84 years old. Well do I remember when a medical student with what profound respect we always raised our hats to this Nestor of our calling, with what courtesy and dignity and cordiality he returned the greeting. One had but to look into his face to see there stamped the marks of the true gentleman, the kindly physician, the enthusiastic student whose only thoughts were for the uplifting of his profession, the benefitting of his fellow creatures, the suppression of evil, and the encouragement of all good works, while all forms of quackery and falsehood found in him a most bitter and persistent opponent.

I now have the pleasure of bringing to your notice one whose influence upon our national medical life has been more potent than that of any other single individual.

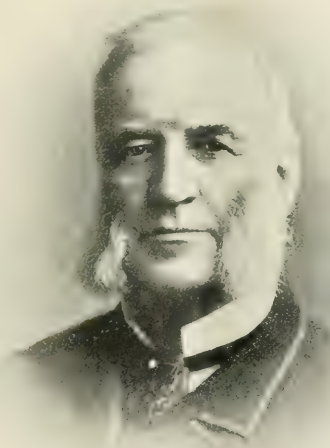
Dr. Austin Flint, born in Petersham, Massachusetts, October 20, 1812, was the fourth of a direct line of distinguished physicians. Educated first at Amherst, he took his degree of Doctor of Medicine at Harvard in 1833 and immediately began active practice in Northampton, then in Boston, but removed to Buffalo in 1836. In 1844 when only 32 years old he was appointed to the chair of Institutes and Practice of Medicine in Rush Medical College, Chicago, and still retained his residence in Buffalo. In 1846 he founded the Buffalo Medical Journal; in 1847 he was one of three to organize the Buffalo Medical College and occupied the chair of professor of medicine; in 1852 he was called to a similar chair in Louisville. In 1856 he returned to Buffalo as professor of pathology and clinical medicine. In 1858 he went to New Orleans to teach clinical medicine and to attend the Charity Hospital. In 1861 he removed to New York to become professor of medicine in Bellevue Hospital Medical College and also of pathology and practical medicine in the Long Island College Hospital. He was also appointed physician to Bellevue Hospital. In these positions he remained during the rest of his life, dying of apoplexy twenty-five years later, in March, 1886, in the seventy-fourth year of his age.

The mere fact of his peregrinations, confined, however, to his own country, gave him a reputation as broad as the nation itself. But not upon these alone does this reputation stand. While teaching he was at the same

time observing and these observations, always true, accurate and careful, were embodied in numerous addresses and publications. Though missing the stimulus of a foreign education he possessed within himself an enthusiasm and a love for study which never tired. It was a positive enjoyment for him to write and once he remarked that "when the work of the day is over I frequently sit in my office and write until eleven, twelve, one or perhaps two o'clock before I feel tired enough to go to bed." His habits were simple, his manners polished; independent and fearless in his opinions; of sterling integrity and spotless in character. No one could come in contact with him without feelings of respect, confidence and love. While by no means confining his attention to diseases of the chest it is to them that he

logical changes otherwise not to be determined from the normal. His Manual on Auscultation and Percussion remained for many years the student's confident guide in these subjects. His influence in offsetting the baleful and reactionary influence of Niemeyer is not to be lost sight of. The latter discarding the doctrine of Laennec that phthisis was dependent upon tubercles, maintained on the contrary that it was due to an haemoptysis or a chronic catarrh, that it should be called therefore a chronic catarrhal pneumonia, and that the danger to the consumptive was that *he might become tuberculous*.

Against these views Flint throws the whole weight of his experience; he analyzes a series of 670 cases and therefrom deduces evidence in support of Laennec's and Louis's ideas.



DR. AUSTIN FLINT.

contributed the greatest amount of knowledge. Particularly was his attention drawn to the study of the physical signs of these diseases and especially to those refinements of auscultatory phenomena which admit of differentiating fine pathological distinctions.

It is he who first proposed the term "cavernous respiration" for the character of the breathing heard over pulmonary cavities, a form of breathing distinctly different from so-called tubular breathing. He also introduced the term "broncho-vesicular respiration" to indicate the breath sounds over areas more or less infiltrated with disease yet not so consolidated as to produce the tubular quality. He especially drew attention to the variation in *pitch* of both percussion and auscultatory sounds indicative of fine patho-

This review is published in book form and is a mine of clinical experience in consumption; many other important deductions are drawn, encouraging alike to the victim of the disease and the practitioner of medicine.

Finally, when 50 years old, he published his treatise on the whole subject of internal medicine. Of it Dr. Jacobi says, "It was the work of a man who had given two dozen years or more to the study of his subject before venturing before the profession with his great book. In his life nobody was more straightforward and honest. What he did not know he would not state and when in the later editions he would make certain chapters more scientific and serviceable by elaborating the pathological anatomy of his themes he selected William H. Welch to write the required chapters and to him he gives full credit in his preface."

The book running through six editions became the standard of medical thought and practice throughout the country. So when in 1865 Villemin demonstrated the inoculability of tuberculosis and in 1881 when Koch disclosed its causative agent, our author, ever progressive and open to sound conviction, threw the weight of his great reputation into the promulgation of these important discoveries and thereby exerted an influence that can never be estimated toward the early and complete acceptance of the new doctrines. Here perhaps more than in any other respect he contributed to the advancement of the study of tuberculosis and is entitled to stand among the foremost students of that disease.

When a half century hence some author undaunted by my attempt pretends to review the history of consumption in this country there are the names of men now living which will stand forth brilliantly on his page.

Flick of Philadelphia quietly but conclusively demonstrating its house infectiousness, through the dried sputum remaining to spread its seeds from one member to another, on from one family to the next to come; Bowditch of Boston proving the efficacy of sanatorium treatment, these two with Knopf, Biggs, Otis, Millet, Baldwin, representing types of many workers.

And yet again who will fail to notice the quiet, patient, often discouraging toil of Trudeau in his isolated laboratory in the heart of the Adirondack mountains, a laboratory the first in this country for the exclusive study of this disease, established by his sole exertions and maintained alone by a devotion to science and a desire for the good of the human race which knows no rebuff—a devotion rewarded fortunately by universal recognition of splendid achievements and by a love which far transcends mere reputation, the love of all his patients and co-workers. May his enthusiasm never fail, nor support for this most beneficial of all works ever be withdrawn!

After this review what may I say as a summary of America's contribution to the study of tuberculosis?

1. That Rush's influence directed men to study in every case the natural history of disease rather than to follow blindly some old world dictum; in his *treatment* of consumption he directed men into the path which with slight deviations is followed still to-day.

2. That Morton first brought back to America Laennec's methods of auscultation for the benefit of his fellow coun-

trymen, inculcating accurate observation and stimulating the study of the morbid anatomy of the disease and spreading the knowledge of it by clear description and accurate illustration. Through his independent investigations he was led to Laennec's and Louis's views, viz., that the *tubercle*, singly or in groups, is the sole pathological expression of tuberculosis.

3. That young Jackson discovered a new auscultatory feature in early pulmonary tuberculosis.

4. That William Gerhard disseminated widely the knowledge of auscultation and percussion and Laennec's pathology of consumption by his repeated publications.

5. That Bowditch demonstrated the pernicious influence of unsanitary surroundings, particularly of soil moisture, on the production of consumption and first illustrated the safe and advantageous use of thoracentesis for pleuritic effusions which so frequently are tuberculous in origin. Moreover, that he was at least one of the first to revive the doctrine of the infectiousness of consumption, and thereupon suggested a mode of treatment which precluded the possibility of its direct transmission.

6. That Austin Flint introduced several auscultatory features of value in determining the pulmonary condition, and by his teachings was beneficial in controverting the retrogressive teachings of Niemeyer. His careful analysis of an unexampled series of cases widened the knowledge of the disease, and his unbounded influence led to the early acceptance, in this country at any rate, of the discoveries of Villemin and Koch.

7. That Flick has demonstrated that the danger lies in the dried sputum collected in infected houses.

8. That Vincent Bowditch and others have proven that in local sanatoria as well as in mountain resorts the consumptive may recover.

9. That Trudeau has experimentally demonstrated the value of pure air in resisting tuberculosis and has assisted in demonstrating the almost complete valuelessness of so-called specific drugs. Furthermore that he has controverted by his experiments much that was false in regard to the value of tuberculin and in other ways greatly added to the knowledge of the treatment of consumption.

10. And finally that many others of our countrymen whose names unfortunately cannot here be mentioned for lack of time, have contributed, by their writings and by their experience, to a fuller understanding of this disease.

## STUDIES IN TYPHOID FEVER.

### SERIES I-II-III.

The papers on Typhoid Fever, edited by Professor William Osler, M.D., and printed in Volumes IV, V and VIII of The Johns Hopkins Hospital Reports have been brought together, and bound in cloth.

The volume includes thirty-five papers by Doctors Osler, Thayer, Hewetson, Blumer, Flexner, Read, Parsons, Finney, Cushing, Lyon, Mitchell, Hamburger, Dobbin, Canac, Gwyn, Emerson and Young. It contains 776 pages, large octavo, with illustrations. It gives an analysis and study of the cases of Typhoid Fever in The Johns Hopkins Hospital for the past ten years.

The price is \$5.00 per copy. Only a few copies of the volume are on sale. Those wishing to purchase should address their orders to the JOHNS HOPKINS PRESS, BALTIMORE, MARYLAND.

AMERICA'S CONTRIBUTIONS TO SURGERY.<sup>1</sup>

MARTIN B. TINKER, M. D.

*Assistant Resident Surgeon, The Johns Hopkins Hospital.*

In my reading of medical literature during the past five years I have kept a list of the occasional references to important achievements of our American surgeons. Looking over this list recently I was surprised to see how great has been the number of these important contributions. Without having gone over the literature to make a systematic search so as to make a complete list of the notable achievements of American surgeons, I shall mention only those which have happened to come to my notice in a moderate amount of reading, together with some which I have found by reference to historical articles. The names included will be those only who have performed some important operation for the first time, introduced new and valuable methods or have made specially important changes in old methods or in some other way have really contributed to the progress of surgery. There will be no doubt, many omissions, but within the limits of a brief paper it is impossible to notice all, and even this incomplete list makes a very remarkable showing for a nation but little over a hundred and twenty-five years old.

**ANÆSTHESIA.**—America can claim one discovery of truly epoch-making importance in surgery: the prevention of pain during operations by general anæsthesia. Anæsthesia and antiseptics are certain to stand through all time as the great medical discoveries, not only of the nineteenth century but of the entire history of surgery. Important as all of us regard antiseptics I feel sure that if we had to choose between operations without anæsthesia or without antiseptics many of us would take the old dirty methods rather than the terrible torture of an operation without anæsthesia. Every member of the medical profession knows of Wm. T. G. Morton who introduced ether anæsthesia in 1846; how after failing in business in Boston, he studied dentistry in Baltimore, and later studied medicine in Boston. How he entered the dental office of Horace Wells, the discoverer of nitrous oxide gas anæsthesia, as an assistant, later becoming Wells's partner; how, while at Harvard Medical School, he was an office student of Charles P. Jackson, the physician and chemist; how after much experimentation on animals, upon himself and upon dental patients he finally established the value of ether anæsthesia. You also are familiar with the long controversies as to whether the credit for the discovery of anæsthesia belonged to Crawford W. Long, of Danielsville, Georgia, who removed a small tumor from a negro's neck under ether anæsthesia, as early as 1842, or to Jackson or Wells, both of whom laid claim

to the credit for this discovery. Sir James Paget<sup>2</sup> has summed up their relative claims very well as follows: "While Long waited and Wells turned back and Jackson was thinking, and those to whom they had talked were neither acting nor thinking, Morton, the practical man went to work and worked resolutely, he gave ether successfully in severe surgical operations, he loudly proclaimed his deeds and he compelled mankind to hear him." Whatever our decision may be as to the relative merits of the claims of these different men they were all Americans, and the credit for the discovery of anæsthesia certainly belongs to an American.

The discovery of anæsthesia marks a new period in the history of surgery. Before this discovery surgery consisted mainly in the treatment of fractures and dislocations, the occasional ligation of arteries, amputations, cutting for stone and the excision of a few small and readily accessible tumors. In this limited field Americans did their full share of original work.

**LIGATION OF ARTERIES.**—Early American operators were specially bold and original in the ligation of the large arteries of the body, and have contributed proportionately more to this field than the surgeons of other nations. In this connection the name of Valentine Mott, of New York, deserves first mention. After studying under Abernethy, Cooper, Charles Bell and Munro, in London and Edinburgh, Mott engaged in practice in New York City. He was the first to tie the innominate artery, May 18, 1818.<sup>3</sup> This carried his reputation to all parts of the civilized world; but that was a small part of his work in the ligation of arteries. Gross, in his Memoir of Mott, published in 1868, says: "No surgeon living or dead ever tied so many vessels or so successfully for the cure of aneurysm, the relief of injury or the arrest of morbid growths." He credits Mott with having tied the femoral artery 57 times, the carotid 51 times, the popliteal 10 times, the subclavian 8 times, the external iliac 6 times, the internal iliac twice and the common iliac once. In all he is said to have ligated great arteries of the body 135 times. Mott's name was also made famous in his day as a daring surgeon, who undertook all kinds of major operations, by his excision of the clavicle for malignant growth for the first time in the history of surgery, for his translation of Velpeau's Surgery, and as one of the leading teachers of that time.

J. Kearny Rogers, of New York, who was born in 1793, and studied in England under Sir Astley Cooper, Abernethy

<sup>1</sup> Read before the Johns Hopkins Hospital Historical Club, February 10, 1902.

<sup>2</sup> Nineteenth Century, December, 1879.

<sup>3</sup> Medical and Surgical Register, New York, 1818, vol. i, p. 9.

and Brodie, made his name famous by first ligating the left subclavian artery between the scapular muscles.<sup>4</sup> Sir Astley Cooper had failed in an operation attempted in 1809. He was the founder of the New York Eye and Ear Infirmary, and a surgeon to the New York Hospital.

The subclavian artery was first tied on the scapular side of the scapular muscles by Wright Post, of New York, then professor of surgery in Columbia University. Post was born at New Hampstead, Long Island, February 19, 1766. When fifteen years of age he was apprenticed to Dr. Richard Bailey, one of the most celebrated and skilful surgeons of that day in New York. After working with Bailey for four years he studied in London under Sheldon, and the celebrated Dr. Bailey devoting special attention to anatomy. He established the first school of anatomy in New York City, which was regarded at that time with such disfavor that he was attacked by a mob at one time soon after its establishment. He was in his day the master surgeon of New York City, and something of his reputation has come down even to the present. Mott, in his memoirs of Post,<sup>5</sup> speaks of his ligation of the subclavian as follows: "But the masterly stroke of Dr. Post in surgery remains to be mentioned. It is certainly for the honor of our time, for the credit of America and for the pride of our city that the first successful operation of tying the subclavian artery above the clavicle on the scapular side of the scapular muscles for an aneurysm was first performed by him. To succeed in an operation of such delicacy and danger which had failed in the hands of such master spirits in surgery as Ramsden, Abernethy and Cooper was a triumph reserved for our friend."

The ligation of the common carotid artery was first done successfully in 1805, by Amos Twitchell, then of Keene, New Hampshire. Twitchell was born in Marlborough, New Hampshire, in 1781. He studied in the common schools, where he fitted himself for Dartmouth College, from which he graduated in 1802. After studying in the recently established medical school of Dartmouth, under the celebrated Nathan Smith, he settled in a small country town in New Hampshire, and there performed the operation which has done most to make his name known. He tied the common carotid artery for secondary hemorrhage following an accidental gun-shot injury at a regimental review. The hemorrhage occurred some days after the injury and the artery was said to have spurted three or four feet, rendering the patient almost absolutely bloodless. It was then taught by surgeons and physiologists that it was unsafe to tie the carotid artery for it was thought that so much of the blood supply to the brain would be cut off that death would immediately result. Twitchell realizing, however, that the only possible salvation of his patient lay in securing the artery compressed it with one hand against the vertebræ, while with the other he dissected it free and with the aid of the patient's mother applied a ligature. Twitchell wrote very

little, and for a long time Sir Astley Cooper was credited with this operation, although, according to Twitchell's biographer, Dr. Albert Smith,<sup>6</sup> Twitchell performed the operation eight months previous to Cooper's first operation, which resulted in the death of the patient. Smith says of this operation: "Thus in an obscure country town, alone, unaided either by counsel or competent assistance, inexperienced and without any preparation, his only help an agitated mother, did he perform with masterly skill and self-possession what was then one great, untried and unsettled operation of surgery."

William Gibson, a native of Maryland, the professor of surgery in the University of Maryland and later from 1818 to 1854, in the University of Pennsylvania, was the first to tie the common iliac artery.<sup>7</sup> Gibson also devised a bandage for fractures of the lower jaw, which is still in quite general use.

Phillip Syng Physick first advised the use of animal ligatures<sup>8</sup> in tying arteries, which he cut close and left buried in the wound. Physick made his ligatures of buckskin, rolling them under a marble slab. There is still considerable discussion as to the advisability of using absorbable ligatures, but there are those who believe that this is an important contribution to surgery. Physick was born in Philadelphia in 1768. He studied four years under John Hunter in London, then returned to set up in practice in Philadelphia. At first he found surgical practice so slow that he contemplated giving it up for farming. He became the first American surgeon of his time, often spoken of as the "Father of American Surgery," and for some time he was professor of surgery in the University of Pennsylvania. Physick advocated rest in the treatment of hip joint disease<sup>9</sup> and Pott's disease, the opposite of what was taught by Brodie, who was then considered the great authority on such subjects. He first reported a case of saciform rectum;<sup>10</sup> he advocated manipulation in the reduction of dislocations and invented the tonsillitome which is now used in many thousands of cases yearly.<sup>11</sup> His operation upon Chief Justice Marshall for stone in the bladder is famous from the large number removed, upwards of 1000, ranging in size from the size of a small shot to that of a bean. Although not a great writer he is among the best known of the earlier American surgeons.

In connection with the ligation of arteries may be mentioned the treatment of aneurysm by digital compression. This was introduced by Jonathan Knight,<sup>12</sup> of New Haven, Connecticut, and professor in Yale Medical School, who

<sup>4</sup> New Hampshire Journal of Medicine, 1850-51, vol. i, p. 287.

<sup>5</sup> American Medical Recorder, 1820, iii, p. 185.

<sup>6</sup> Eclectic Repertory, Philadelphia, 1816, vol. vi, 391.

<sup>7</sup> Paper by Randolph, American Journal of the Medical Sciences, 1830-31, vii, 299.

<sup>8</sup> American Cyclopaedia of Practical Medicine and Surgery, vol. ii, p. 123.

<sup>9</sup> American Journal of the Medical Sciences, 1827, vol. i, 262.

<sup>12</sup> Boston Medical and Surgical Journal, 1845, vol. xxxviii, 293.

<sup>1</sup> New York Journal of Medicine, 1846, vol. vi.

<sup>2</sup> Transactions of the Medical Society of New York, 1828, p. 18.

succeeded in curing a popliteal aneurysm in this way. John Mason Warren, of Boston, also treated two inoperable aneurysms of the subclavian artery successfully by compression applied with weights directly over the aneurysmal tumor.<sup>12</sup>

**DISLOCATIONS.**—Up to about fifty years ago dislocations were commonly treated by a barbarous system of pulleys and forcible extension, although manipulation had been recommended by several surgeons from the days of Hippocrates to Nathan Smith, who practised manipulation successfully in reduction of dislocations.<sup>13</sup> Dr. Wm. W. Reid, of Rochester, New York, was the first to make a thorough study of the subject and to show by a series of dissections, experiments and observations the desirability of reducing dislocations by this method. His paper shows a high degree of originality and thoroughness, and deserves to be better known. Physick and Smith have already been mentioned in this connection and the work of Bigelow, of Boston,<sup>14</sup> in the reduction of the hip joint by this method is too well known to need mention. Many who know of the method of putting the hand on the opposite shoulder and trying to bring the arm to the side to determine the diagnosis in dislocations of the shoulder do not know that this method originated with L. A. Dugas,<sup>15</sup> a prominent practitioner of his time in Georgia.

**EXCISIONS OF BONES AND JOINTS** had been practised in certain cases long before the settlement of America, but it remained for Horatio G. Jameson, a Baltimorean, in 1820, to first excise the upper jaw.<sup>16</sup> Gross, in discussing this subject states that many others had chipped off pieces of the superior maxilla, but Jameson was the first to remove the entire jaw with exception of part of the roof of the antrum in 1820.

Excision of the lower jaw was first performed by Deaderick, of Rogersville, Tennessee, in 1810, although his report of the operation did not appear until many years later.<sup>17</sup> The operation was performed for a large enchondroma involving the entire inferior maxillary bone and filling the mouth completely. The patient made a good recovery and was reported well thirteen years after the operation.

Valentine Mott first excised the clavicle for malignant growth in the days before the introduction of anæsthesia, the operation lasting four hours, forty vessels requiring ligation.

John Warren, of Boston, brother of General Joseph Warren, of Bunker Hill (also a successful physician), a surgeon in the Continental Army, and the first professor of surgery

in Harvard University, first excised the parotid in 1804.<sup>18</sup> It is mainly through George McClellan, of Philadelphia, that this operation was introduced into surgery. McClellan was born in Woodstock, Connecticut, in 1796. He graduated from Yale College, where he was a favorite student in science of Professor Silliman. He then studied medicine under a preceptor, and at the University of Pennsylvania. Settling in Philadelphia, he was early distinguished as a bold and daring operator, a fascinating and enthusiastic teacher, the founder of Jefferson Medical College of Philadelphia and the author of a text-book on the Principles and Practice of Surgery. He is reported to have excised the parotid 11 times,<sup>19</sup> and he was among the first to amputate the entire upper extremity for malignant growth. He shared with Mott, of New York and Warren of Boston the credit of establishing many procedures new in America. Interseapulo-thoracic amputation or removal of the entire upper extremity must have been a most heroic operation in the days before the introduction of antisepsis. Dr. Dixie Crosby of Hanover, New Hampshire, was the first to perform this operation in 1836.<sup>20</sup> His patient lived 28 months and is said to have died with paraplegia, probably as a result of metastases of the growth to the lumbar spine. Crosby was among the first professors of surgery in Dartmouth Medical College and one of the boldest and most famous operators of his time.

**ABDOMINAL SURGERY** practically had its origin in America with Ephraim McDowell's first ovariectomy which was performed in 1809. He afterwards operated in 13 cases with 8 recoveries. This is one of the few operations first performed by American surgeons for which credit is generally given. McDowell was a Virginian by birth; he was educated at the University of Edinburgh, studying under John Bell, and he practiced in what was then a small frontier town, Danville, Kentucky. Besides ovariectomy he did numerous other surgical operations and is said to have been specially successful as a lithotomist.

Nathan Smith performed a successful ovariectomy in 1821 without knowledge of McDowell's operation, tying the stump with leather ligatures said to have been cut from a buckskin glove. Smith is another of the few early American surgeons whose reputation has come down to the present time. He was born in Rehoboth, Massachusetts, in 1762, but his family moved to Vermont while he was young and he was a member of Vermont militia during the latter part of the Revolution. He gained a limited education in the country schools and was chiefly occupied on his father's farm until he was 24 years old, when, after witnessing a surgical operation, he determined to study medicine. After some preliminary instruction he studied three years as an office pupil of Dr. Goodhue of Putney, Vermont. He then practiced for

<sup>12</sup> Surgical Observations, Boston, 1867, p. 424.

<sup>13</sup> Medical and Surgical Memoirs of Nathan Smith, page 163, published after his death in 1831.

<sup>14</sup> The Hip, Philadelphia, 1869.

<sup>15</sup> Southern Medical and Surgical Journal, 1856, xii, 131.

<sup>17</sup> American Medical Recorder, Philadelphia, 1831, vol. iv, 222.

<sup>18</sup> American Medical Recorder, Philadelphia, 1823, vol. vi.

<sup>19</sup> Mentioned in Surgical Observations, J. M. Warren, Boston, 1867, 288.

<sup>20</sup> McClellan's Surgery, Philadelphia, 1848, p. 364.

<sup>21</sup> Full report given in monograph by his son A. B. Crosby, Concord, New Hampshire, 1873.

two or three years, studied at Harvard Medical School where he graduated as Bachelor of Medicine; later he studied under Munro in Edinburgh and visited the London hospitals. He has been justly considered one of the most extraordinary medical men this country has ever produced, whether we regard his great ability as a general practitioner, his skill and daring as a surgeon or his versatility as a teacher of the different branches of medicine. Smith was one of the founders of Dartmouth, Yale and Bowdoin Medical Colleges. He wrote one of the most important articles on typhoid fever which had appeared;<sup>22</sup> he advocated manipulation in the reduction of dislocations and trephined for osteomyelitis long before this operation was suggested by Brodie, who is commonly credited with this operation.

After the introduction of anesthesia the progress in abdominal surgery was of course far more rapid. Before this society last year I presented the claims of Wolcott of Milwaukee for the first nephrectomy and of Bobbs of Indianapolis for the first cholecystotomy.<sup>23</sup> In addition to these operations nearly all of the mechanical methods of intestinal anastomosis which are in much favor among prominent surgeons, were introduced by Americans, also the importance of taking in the submucosa in the suture method of intestinal anastomosis. But these methods of Halsted, Murphy, Senn, Leplace and O'Hara are of such recent introduction that they are well known to everyone.

APPENDICITIS. American surgeons have done more to show the importance of operative treatment of appendicitis than the rest of the world put together and in this way have been instrumental in saving thousands of lives. In 1867 Willard Parker<sup>24</sup> of New York showed as the result of his experience that early operation would save 75 per cent of all cases.<sup>25</sup> He advocated operation on the fifth to the twelfth day. Fitz of Boston, though not a surgeon, by his exhaustive study of this subject and his advocacy of early operation did as much as any one to bring about the views now generally accepted. Thomas G. Morton reported at the thirty-ninth meeting of the American Medical Association a case of appendicitis operated upon in April, 1887, which was probably the first appendectomy on record. MacBurney besides contributing to the operative technique and diagnosis by his successful records has done much to bring this operation into prominence. These are only a few of the many American names deserving honorable mention in this connection. It is strange that in Germany, England and France many of the best known surgeons still have not advanced further than had Willard Parker over thirty years ago and only a few of the most progressive surgeons of European countries have come to adopt the treatment which has been proved by experience of twenty years in America to save most lives.

One of the most important advances in the treatment of fractures was the use of extension apparatus. This method was first brought before the profession by Gross,<sup>26</sup> who states that his preceptor, Joseph K. Swift of Easton, Pennsylvania, was the first to use it. Gurdon Buck<sup>27</sup> of New York deserves great credit for introducing the well-known apparatus for treatment of fractures of the femur, however, which is commonly known as Buck's extension. In his paper he reports his results including measurements in 21 cases.

PLASTIC SURGERY. In plastic surgery John Mason Warren of Boston deserves special mention.<sup>28</sup> He was the grandson of John Warren and father of the present professor of surgery in Harvard University, a member of that notable surgical family that has furnished Harvard with professors and Boston with surgeons for nearly two hundred years. He was the first to do the plastic operation on the hard palate now known as uranoplasty in 1843 and had a record of 24 cases of this kind with only one failure, unusually brilliant even at the present day. He performed staphylorrhaphy for defect of the soft palate one year after Roux of Paris, but quite independently, and is said to have operated on over 100 cases of this kind, most of them very successfully. Velpeau also credits Warren with having been the first to puncture the pericardium for the relief of effusion, a procedure considered by most surgeons of that time as almost certainly fatal and unjustifiable.<sup>29</sup> Warren also performed many successful rhinoplastic and harelip operations which he reports in his *Surgical Observations*.

Joseph Pancoast of Philadelphia was the first to do a successful operation for extrophy of the bladder, still considered a very difficult condition to treat. His paper was published in 1859.

Skin grafting was probably first suggested by Hamilton, then of Buffalo, in 1847. In 1854 he reported a case in which he had successfully grafted a large raw surface caused by a heavy stone falling on a man's leg. Hamilton is perhaps best known from his book on fractures.

MISCELLANEOUS BRAIN operations were very seldom performed except for fractures of the skull before the time of the introduction of anesthesia. Benjamin Winslow Dudley deserves mention as one of the first modern surgeons to successfully trephine for the relief of epilepsy. He operated upon his first case in 1819 and afterward reported six successful cases<sup>30</sup> of trephining for this condition. Most of these operations were for traumatic epilepsy. Dudley was also a famous lithotomist, having operated upon 207 cases with the loss of only six patients. Dudley was born in Virginia in 1785. He studied in London under Sir Astley Cooper, Abernethy and Klein; in Paris under Baron Larrey

<sup>22</sup> Autobiography, vol. 1, p. 99.

<sup>23</sup> Bulletin in New York Academy of Medicine, 1860-62, vol. 1, 181.

<sup>24</sup> American Journal of the Medical Sciences, 1843, N. S., vi, 257 and *Ibid.*, 1848, N. S., xv, 329.

<sup>25</sup> Mott's American Edition of Velpeau, Operative Surgery, 1847, vol. iii, p. 520.

<sup>26</sup> American Journal of the Medical Sciences, 1832, vol. xi, p. 542.

<sup>27</sup> "A practical essay on typhous fever," New York, 1824.

<sup>28</sup> Johns Hopkins Hospital Bulletin, 1901, xii, 247.

<sup>29</sup> Medical Record, 1867, vol. ii, p. 25.

<sup>30</sup> American Journal of the Medical Sciences, 1836, N. S., vol. xcii, p. 321.

and Boyer. He was professor of surgery in Transylvania University, Lexington, Kentucky, and he performed successfully practically all of the operations in surgery which were known in his day.

In 1858 Carnochan of New York<sup>31</sup> reported his method of *resection of the superior maxillary nerve beyond Meckel's ganglion for neuralgia*.

In 1849 Detmold of New York first evacuated a brain abscess.

Hartley of New York devised the method for *removal of the Gasserian ganglion* which has been in most general use and Americans have performed nearly half of the entire number of all these operations thus far reported.

By reference to v. Bergmann's extensive tables of *operation for brain tumor* I find that nearly one-third of something over 300 cases of brain tumors thus far reported have been operated upon by American surgeons with a proportionately large number of successful cases.

As an organizer of the profession as well as a most eminent surgeon Samuel D. Gross stands among the first. He was born near Easton, Pennsylvania, July 8, 1805. Of Pennsylvania German parentage, he could speak hardly English when he was 15 years of age. He began the study of medicine when but 19 years old under a preceptor, but realizing his lack of fundamental education he gave up the study of medicine to enter an academy at Wilkesbarre, later taking up the study of medicine in the Jefferson Medical College, where he graduated in 1828. Soon after his graduation he entered upon his career as a teacher, first as demonstrator of anatomy at the Medical College of Ohio in Cincinnati, then as professor of surgery at the University of Louisville, Kentucky, at the University of New York, and at the Jefferson College of Philadelphia. It was largely through his influence that the American Medical Association, the American Surgical Association and the Academy of Surgery in Philadelphia were organized. By his writings, specially by his volume on surgery which was translated into a number

of foreign languages he brought American medicine to the notice of Europeans almost for the first time. This led to a recognition then almost, if not quite, unheard of at that day, honorary degrees from Oxford, Cambridge and Edinburgh, as well as membership in many foreign societies. Although his name is not connected with any special operation he must be considered one of the most eminent surgeons America has produced.

To sum up a few of these achievements of American surgeons which I have mentioned:

1) The introduction of general anæsthesia. 2, 3, 4, 5) Four of the most difficult ligations of arteries (innominate, common carotid, common iliac, subclavian, scapular side of scaleni. 6) Introduction of animal ligatures. 7) Treatment of aneurysm by compression. 8) Nephrectomy. 9) Cholecystotomy. 10) Ovariectomy. 11) Introduction of nearly all methods of intestinal anastomosis now in use. 12) The introduction of the proper treatment of appendicitis. 13) Excision of the parotid. 14, 15, 16, 17) Four important excisions of bones (superior and inferior maxillae, clavicle, interscapulo-thoracic amputation). 18) Operation for osteomyelitis. 19) Drainage of brain abscess. 20) Manipulation in the reduction of dislocations. 21) Skin grafting. 22) Closure of defects in cleft palate. 23) The invention of the tonsillitome

My excuse for presenting this paper is not that the facts are entirely unknown or inaccessible but the belief that even those familiar with the work of individuals may not realize how large the sum total of the contributions of American surgery has been. Many American surgeons are quite familiar with the work of foreigners but lamentably ignorant of that of their own countrymen. This is partly due to the fact that the Germans, French and English seem to take much more pride in achievements of their countrymen than we do in America, and partly because many in our country have neglected to properly record and report their cases. If we do not take pride in our own work we cannot fairly expect others to do so.

## THE TOXICITY OF METHYL ALCOHOL.

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The number of cases of poisoning by methyl (or wood) alcohol has greatly increased in the last few years; this is due very largely to the fact that wood alcohol is now frequently used as a constituent of certain preparations where ethyl (or grain) alcohol was formerly employed. Not only have preparations intended for use in the arts (as varnishes, etc.) or for external use (as bay rum) been made with methyl alcohol as an ingredient, but even medicinal or flavoring agents (essence of Jamaica ginger, pepper-

mint, etc.) intended for internal use have been found to contain it. The use of methyl alcohol in the latter class of preparations has attracted the attention of the medical profession to this substance, as many deaths have resulted from the use of these preparations; and the leading ophthalmologists of this country and of Europe are agreed in ascribing many cases of total or partial blindness to the wood alcohol contained in them.

While much has been written concerning the action of

<sup>31</sup> American Journal of the Medical Sciences, 1858, vol. xxxv, p. 134.

methyl alcohol upon the eye and considerable experimental work has been done upon this subject (notably by Friedenwald and Birch-Hirschfeld), very little has been published recently concerning the general physiological action of methyl alcohol and the points in which this differs from the action of the much better known grain alcohol. Although it has been known to pharmacologists for many years that the action of methyl alcohol is, in some respects, so markedly different from that of ethyl alcohol that the substitution of the former for the latter in any preparation intended for internal use (especially if the preparation were to be taken for some time) would inevitably be accompanied by the greatest danger,<sup>1</sup> there seems to be much ignorance of this fact even among physicians; this probably results from the fact that little or nothing is said about methyl alcohol in some of the leading English text-books on toxicology (which, as a rule, discuss only those poisons which have already been of medico-legal interest). The subject is discussed, however, in all of the leading German text-books on toxicology. Under the circumstances a brief resumé of our knowledge of the general physiological action of methyl alcohol may be of interest; a number of experiments of my own upon animals will also be described.

There are two forms of methyl alcohol poisoning, acute and chronic. While the chronic, or still more, the sub-acute form is the one of greater interest (since it differs markedly from poisoning by grain alcohol), a few words may be said about the acute form.

#### ACUTE POISONING WITH METHYL ALCOHOL.

The symptoms of acute poisoning of animals with methyl alcohol are, in general, similar to those observed in cases of poisoning by ethyl and other alcohols of this series. These symptoms are too familiar to require description here. The action of methyl alcohol differs from that of ethyl alcohol chiefly in the fact that the symptoms are produced more slowly and the duration of the intoxication is more prolonged. Thus the state of coma does not appear, as was shown by Joffroy and Serveaux, for some little time even when methyl alcohol is injected directly into the vein of an animal, whereas after the injection of ethyl alcohol it appears with great rapidity. The coma caused by methyl alcohol continues for a very much longer time than does that caused by ethyl alcohol; thus it is not uncommon for the coma in the former case to continue for two, three or even four days, whereas that caused by ethyl alcohol may not continue for more than six hours and, in the numerous experiments of Joffroy and Serveaux, was never observed to continue for twenty-four hours.

Similar differences between the action of methyl and ethyl alcohols are well known in the case of man, but there is a tendency to explain the long continued narcosis caused by the former to the presence of various impurities; no

support for this view has been offered and numerous experiments on animals with pure methyl alcohol have shown that the long continued after-effect is due to a property inherent in the methyl alcohol itself.

Among the various symptoms caused by methyl alcohol in animals, Joffroy and Serveaux (*Arch. de Méd. expér.*, viii, p. 490) called attention to the marked fall of body temperature and to the partial loss, on the part of the animal, of the power to regulate its temperature according to that of the surrounding air. There are marked changes in the alimentary tract; thus hemorrhages, leading to bloody diarrhoea or to the vomiting of bloody matter, are of frequent occurrence. There are convulsions or convulsive movements of a rhythmic or choreiform character, often continuing for a day or two and followed, finally, by a loss of sensation and of reflex movement; the corneal reflex, however, may persist for a long time. Joffroy and Serveaux also call attention to the marked convulsive movements of the eyes; these often constitute nystagmus of a pronounced type. This nystagmus usually occurs spontaneously, but when it is absent it can be caused very easily by simply moving the head of the animal; there are first convulsive movements of the eyes followed by a nystagmus, at first rapid, then slow. There is usually dilatation of the pupil.

Perhaps the point of greatest interest in connection with the subject of acute poisoning by methyl alcohol is the question of the relative toxicity of methyl and ethyl alcohols, i. e., the relative quantities which, when administered in a single dose to an animal, will cause death in a short time. All who have investigated this subject experimentally are agreed that there is but little difference between the toxicity of the two alcohols in cases of acute intoxication. Some of the earlier writers ascribed slightly greater toxicity to methyl alcohol; thus Dujardin-Beaumetz and Audigé (*Comptes rend.*, 83, p. 80, 1876) placed the lethal dose of methyl alcohol, injected subcutaneously into dogs, at 7 gr. per kilogramme body weight, the lethal dose of ethyl alcohol being, according to these authors, 7.75 gr. per kilogramme. Later writers ascribe a slightly greater toxicity to ethyl than to methyl alcohol. Thus Joffroy and Serveaux in their classical studies on the toxicity of methyl alcohol found the "true toxic equivalent" of methyl alcohol (i. e., the quantity per kilogramme body-weight which, when injected into a vein or into the muscular tissue, would almost always lead to death within a short time—a day or two) to be, for the dog, about 9 ccm. (7.2G.); for the rabbit the dose was about 10 ccm. (7.96G.). The figures were the same whether the "pure methyl alcohol" of commerce or whether chemically pure methyl alcohol was employed. These authors (*Arch. de Méd. expér.*, ix, p. 707) found the true toxic equivalent of ethyl alcohol to be, for the dog, 8.65 ccm. (6.92G.), for the rabbit, 8.15 ccm. (6.52G.). The toxicity of the "pure ethyl alcohol" of commerce was slightly greater, being 6.86 G. for the dog and 6.20G. for the rabbit.

<sup>1</sup> This has been the teaching of Professor Abel, for example, ever since the opening of the Johns Hopkins Medical School in 1893.

Baer (Archiv f. Anat. u. Physiol., 1898, p. 289) experimenting on rabbits and introducing the diluted alcohols into the stomach, placed the toxic dose of methyl alcohol at from 7.2 to 9G. per kilogramme body-weight, that of ethyl alcohol at 6.25 to 7.44G.

The slight discrepancies between the results of the authors quoted above can be easily explained by the differences in the methods of experimenting; some authors administered the alcohol intravenously or injected it directly into the muscles, others gave it by the stomach. In some experiments dogs, in others rabbits were used. Indeed it is remarkable that the results have been so uniform when these facts are considered. The above results also show that the various specimens of wood alcohol used in the experiments must have been comparatively pure or that the impurities commonly present in wood alcohol have but little toxic action, for it is highly improbable that the same impurities should occur, and occur in the same quantity, in specimens of wood alcohol obtained at such different places and at such intervals of time.

My own experiments on the subject of acute poisoning were limited to a few observations on the fatal period after the administration, in one or two doses, of equal quantities of methyl and ethyl alcohols. The description of the symptoms will be omitted as there was nothing especially noteworthy.

The preparation of methyl alcohol used in most of the experiments was Kahlbaum's purest methyl alcohol; it was perfectly colorless, entirely free from acetone and other substances giving an iodoform reaction. The specific gravity and boiling point corresponded to methyl alcohol of about 99.6 per cent. The ethyl alcohol used, as a rule, was Squibb's absolute alcohol. The alcohols were diluted with water and introduced into the stomach by means of a soft rubber catheter.

In the first two experiments the dose was 10G. per kilogramme animal.

I. Experiment with methyl alcohol, May 15th. Male rabbit, weighing 2.28K. At 4.55 p. m. a mixture of 22.8G. of methyl alcohol and 68.4G. warm distilled water administered. The animal was soon deeply intoxicated and died on the following afternoon at about 5 o'clock, that is 24 hours after the alcohol was given.

II. Experiment with ethyl alcohol, May 15th. Female rabbit, weighing 2.17K.

5-10 p. m., 21.7G. of ethyl alcohol diluted with 65G. of warm distilled water administered. The animal had convulsions of a mild type in 15 minutes and died at 11 p. m., that is 6 hours after the poison was given.

In the two following experiments both the methyl and ethyl alcohols were diluted to 89 per cent (by weight) and 16G. per kilogramme body-weight of the diluted alcohol was mixed with water and given to the rabbits in two doses; these corresponded to about 14.2 G. of the pure alcohols.

III. Experiment with methyl alcohol, May 16th. Male rabbit, weighing 1.75K.

10 a. m., 14G. of 89% methyl alcohol diluted with 42G. of distilled water given by the stomach.

May 17th, 1.50 p. m. The above dose was repeated.

May 18th. The animal was living but seemed to be at point of death.

May 19th, 7 a. m. The animal has apparently been dead for many hours.

The animal died in from 56 to 69 hours after the first dose.

IV. Experiment with ethyl alcohol, May 16th. Male rabbit, weighing 1.84K. 9.40 a. m., 14.7G.<sup>1</sup> of 89% (92.4% by volume) ethyl alcohol diluted with 45G. of distilled water administered.

May 17th, 1.45 p. m. The above dose was repeated.

May 18th. The animal died about 11 a. m., i. e., about 49 hours after the administration of the first dose.

In the following two experiments the pure alcohols were given in two doses of 6.5G. each, per kilogramme body-weight.

V. Experiment with methyl alcohol, May 16th. Female rabbit, weighing 1.8K.

4.10 p. m., 11.7G. pure methyl alcohol diluted with 35G. distilled water administered.

May 17th, 2 p. m. The above dose was repeated. Convulsive movements of the legs and marked nystagmus were noticed soon afterwards.

May 18th. The animal was alive at 6 p. m.

May 19th. The animal has apparently been dead for many hours.

The rabbit died between 74 and 84 hours after the administration of the first dose.

VI. Experiment with ethyl alcohol, May 16th. Male rabbit, weighing 1.45K.

4 p. m., 9.4G. ethyl alcohol diluted with 28G. distilled water administered.

May 17th, 2.5 p. m. The above dose was repeated.

May 18th. The animal lived throughout the day.

May 19th, 7 a. m. The rabbit was found dead. The animal died between 50 and 60 hours after the administration of the first dose.

The above experiments show that with equal doses of ethyl and methyl alcohols death is caused in a shorter time by the former than by the latter; this agrees with the generally accepted view that in acute poisoning ethyl alcohol is slightly more toxic to dogs and rabbits than is methyl alcohol.

In the following two experiments the methyl alcohol used was a commercial preparation known as Columbian Spirits; it was not the purest preparation known by this name, but was of a light yellow color and gave a fairly well marked iodoform reaction (acetone?). The specific gravity was 0.802 (at 15.5° C.), which would correspond to about 98 per cent pure methyl alcohol, provided that only methyl alcohol and water were present.

VII. Experiment with Columbian Spirits, June 23d. Rabbit weighing 1.2K.

2 p. m., 12G. Columbian Spirits diluted with 36G. water administered.

<sup>1</sup>This dose, which corresponds to 7.1G of absolute ethyl alcohol per kilogramme body-weight is just about the minimal lethal dose, i. e. most rabbits would probably have died from it.

June 24th. The animal is in the deepest coma and seems barely alive.

June 25th. Animal conscious and able to crawl about a little; living at midnight.

June 26th, 6 a. m. Dead. Died between 58 and 64 hours after the alcohol was given.

In this experiment the animal lived much longer than did the one which received an equal dose of pure methyl alcohol (see Experiment I); whether this was due to the fact that the Columbian Spirits contained a slightly smaller percentage of methyl alcohol or to greater resistance on the part of this animal or to the fact that this experiment

ponding doses of pure methyl alcohol and so may be looked upon as offering some confirmation of the view that in acute intoxication the former is slightly more toxic for the lower animals than is the latter.

The question which of these alcohols is the more poisonous to man in acute cases, i. e., which would cause death in the smaller quantity, is a very difficult one to answer. Even the minimal fatal dose of ordinary alcohol for man is not known with anything like the accuracy with which it is known for the lower animals; still less is known in regard to methyl alcohol. The question is further complicated by the fact that a fairly large percentage of the

Date.	Alcohol.	Animal.	Weight of animal.	Quantity of alcohol given.	Dose per kilogramme.	Number of doses.	Result.	Remarks.
I. May 15th.	Kahlbaum's purest, acetone free methyl alcohol.	Rabbit.	2.28K.	22.8G. alcohol, 68.4G. water.	10G.	1	Death in 24 hours.	
II. May 15th.	Absolute ethyl alcohol.	Rabbit.	2.17K.	21.7G. alcohol, 65G. water.	10G.	1	Death in 6 hours.	
III. May 16th.	Kahlbaum's purest methyl alcohol diluted to 89% (by weight).	Rabbit.	1.75K.	28G. alcohol, 84G. water.	16G.	2	Death 56 to 69 hrs. after first dose.	Interval between doses 27 hours 50 minutes.
IV. May 16th.	Pure ethyl alcohol, 89% by weight; 92.4% by vol.	Rabbit.	1.84K.	29.4G. alcohol, 90G. water.	16G.	2	Death 49 hours after first dose.	Interval between doses 28 hours.
V. May 16th.	Kahlbaum's purest methyl alcohol.	Rabbit.	1.80K.	23.4G. alcohol, 70G. water.	6.5G.	2	Death 74 to 84 hrs. after first dose.	Interval between doses 21 hours 50 minutes.
VI. May 16th.	Absolute ethyl alcohol.	Rabbit.	1.45K.	18.8G. alcohol, 56G. water.	6.5G.	2	Death 50 to 60 hrs. after first dose.	Interval between doses 22 hours 5 minutes.
VII. June 23d.	Columbian Spirits.	Rabbit.	1.2K.	12G. Col. Spirits, 36G. water.	10G.	1	Died in 58 to 64 hours.	
VIII. May 16th.	Columbian Spirits.	Rabbit.	1.81K.	29G. Col. Spirits.	16G.	2	Died 32 to 44 hours after first dose.	Interval between doses 28 hours 25 minutes.

was performed in warmer weather than was the one with pure methyl alcohol it is impossible to state.

In the second experiment the Columbian Spirits was given in two doses of 8G. per kilogramme body-weight.

VIII. Experiment with Columbian Spirits, May 16th. Male rabbit, weighing 1.81K.

9.45 a. m., 14.5G. Columbian Spirits diluted with 45 G. distilled water administered.

May 17th. The above dose was repeated. The animal was living at 6 p. m.

May 18th, 7 a. m. The rabbit was found dead, having died between 32 and 44 hours after the administration of the first dose.

The results of the above experiments are shown in the table above:

The above experiments show that death is caused more rapidly by one or two large doses of ethyl than by corres-

ponding doses of pure methyl alcohol and so may be looked upon as offering some confirmation of the view that in acute intoxication the former is slightly more toxic for the lower animals than is the latter.

There are also other considerations which make the pharmacologist hesitate in concluding from these experiments on the lower animals that ethyl alcohol is more toxic to man than is methyl alcohol. The organs most powerfully affected by methyl alcohol are the most highly differentiated nervous structures as is shown by the deep and prolonged coma and in man and the monkey by blindness (due to degenerative changes in the nerve elements of the retina and of the optic nerve). Even in the rabbit the coma is much more prolonged after methyl than after ethyl alcohol. Now it is a well recognized fact in pharmacology that poisons which affect the highly differentiated nerve structures very powerfully are proportionately more dangerous the

more highly developed the nervous system of the animal; hence it would be expected that man would be relatively more susceptible to such a poison as methyl alcohol than would the dog or rabbit.

Under these circumstances it would not be safe to conclude that because ethyl alcohol is slightly more toxic, in acute poisoning, to the lower animals than is methyl alcohol, the same would be true in the case of man. As a matter of fact, a number of cases are reported in which men died from methyl alcohol when equal quantities of ethyl alcohol could almost certainly have been taken with impunity. Physicians who have had extensive hospital experience state that very few of those who are brought to the hospital intoxicated with wood alcohol recover. One explanation often offered for this apparently greater toxicity of methyl alcohol is that the commercial preparations of wood alcohol contain impurities which greatly increase the toxicity; there is little evidence, however, that this is true of any of the preparations of wood alcohol accessible to the public.

In the above discussion the toxicity of the two alcohols has been considered only so far as life is concerned. It is certain that some organs are much more susceptible to the injurious action of one alcohol than to that of the other. That this is the case with the eye, for example, is clearly shown by the cases of wood alcohol blindness in man. As Birch-Hirschfeld expresses it, these cases show that methyl alcohol is capable of injuring the eye to a far greater extent, and also in smaller doses, than is ethyl alcohol; thus cases are reported in which blindness occurred in the most acute form of methyl alcohol intoxication and also after very small doses, a result which probably never occurs with ethyl alcohol.

#### CHRONIC POISONING WITH WOOD ALCOHOL.

The fact that the effects of a single dose of methyl alcohol are long continued suggests that it would be an especially dangerous substance to give at short intervals for any length of time, for it may readily be supposed that under these circumstances the effect of the first dose would not have disappeared when the second was given, and so on. In this way a form of cumulative action would result depending, probably, on the retention within the body of methyl alcohol or of some of its decomposition products. As a matter of fact, all who have investigated this subject have found such a result to be produced, so that methyl alcohol which when taken in a single dose is, as a rule, no more dangerous (at least to the lower animals) than an equal amount of ethyl alcohol, becomes, when its use is continued for even a short time an extremely dangerous poison.

Pohl, in his well known work on the oxidation of alcohol in the animal body (*Archiv f. Exper. Path. u. Pharm.*, 31, p. 281; 1893), stated that chronic poisoning by methyl alcohol is markedly different from that caused by ethyl and other alcohols of this series.

While ethyl and isobutyl alcohols and even amyl alcohol (fusel oil) could be given to animals (dogs and rabbits) in doses sufficient to cause intoxication for months (and even for almost a year) without causing marked anatomical or functional disturbances, methyl alcohol given in small doses every other day was tolerated for but a few weeks; the animals remained comatose for days, did not eat and died, although the administration of the alcohol was discontinued. Extensive fatty degeneration of the liver was always found; thus in one experiment the ether extract (consisting largely of fat) of the dried liver of a dog poisoned by methyl alcohol was 37.7 per cent, while that of the liver of the control (normal) animal was but 16.6 per cent.

Joffroy and Serveaux, the most experienced investigators on the subject of the toxicity of the various alcohols, also lay great emphasis upon the extraordinary toxicity of methyl alcohol in chronic poisoning; they found that it was not only much more poisonous than ethyl alcohol, when given for some time, but that animals could tolerate comparatively large doses of furfural for longer periods than they could methyl alcohol. These authors conclude that it is not possible to foretell the toxicity of an alcohol in chronic poisoning from experiments on acute poisoning.

The great toxicity of methyl alcohol in chronic or sub-acute poisoning is well illustrated by some recent experiments of Birch-Hirschfeld (*v. Graefe's Arch. f. Ophthal.*, liv, p. 68). This writer, who was investigating the effects of methyl alcohol upon the retina and optic nerve, speaks of the difficulty he experienced in keeping the animals alive for even short periods when small doses of methyl alcohol were administered at short intervals. The experiments of Birch-Hirschfeld upon monkeys are of especial interest since these animals react towards narcotic poisons in much the same way as does man; and also because the effect of the poison upon the eye can be studied to far better advantage upon monkeys than upon dogs and rabbits. Birch-Hirschfeld describes experiments upon three monkeys; pure methyl alcohol, diluted with several times its volume of water, was given in doses of from three to six or seven c. cm. every one or two days. When it became evident that the animals were at the point of death they were killed in order that the eyes and optic nerves could be obtained in good condition for microscopical study. The first monkey received 28 c. cm. of methyl alcohol in this way and was in a dying condition on the eighth day; the second animal was moribund on the fifteenth day after having received 79 c. cm. of the alcohol, while the third animal was in a dying condition on the eleventh day after having been given 56 c. cm. of the alcohol. Two of the monkeys had marked degenerative changes in the retina and one was totally blind. Similar histological changes were found in the retinas of three dogs poisoned by methyl alcohol, although it had not been possible to detect disturbances of vision during life.

It is very interesting to compare the above results of

Birch-Hirschfeld with those obtained by de Schweinitz (*Toxic Amblyopias*, p. 51; 1896) in an experiment with grain alcohol. De Schweinitz gave a small monkey (weight eight pounds) an average daily dose of 3.75 c.cm. of 95 per cent grain alcohol for over six months; at times as much as 7.5 c.cm. of alcohol was given every day for several days in succession. The animal was repeatedly very drunk but showed no symptoms of permanent injury and no indications whatever of disturbances of vision could be made out. The animal was finally killed and the eyes and optic nerves were examined microscopically; no degenerative or inflammatory changes were found.

Holden (*Arch. of Ophthal.*, 28, p. 129) reports an interesting experiment in which a form of chronic or subacute poisoning resulted from two large doses of methyl alcohol. A dog weighing ten kilogrammes was given 50 c.cm. of wood alcohol diluted with an equal quantity of water; this dose was repeated five days later. The dog died eleven days after the second dose; the ganglion cells of the retina showed degeneration changes.

*The Writer's Experiments on Subacute Poisoning.*—I have performed a number of experiments upon dogs and rabbits in connection with the question of subacute poisoning by methyl alcohol. Special attention was given to the subacute form of poisoning (i. e., that form in which comparatively large, but not immediately fatal, doses were given at short intervals), as this is the form of poisoning seen most often in man; in a number of the cases of methyl alcohol poisoning in man in which death or blindness has resulted, there has been a history of a "spree" continuing for several days. My attention was directed largely to a comparison of the general physiological effects produced by equal doses of methyl and of grain alcohols. But little attention was given to the influence of the alcohols upon vision, for, as is well known, it is very difficult to determine with much accuracy the effects of drugs upon the sight of dogs and rabbits. In most of the experiments upon dogs, however, a purulent or fibrino-purulent conjunctivitis was noticed and in at least one case the animal seemed to be blind.

Most of the experiments were performed in groups of two; to one animal methyl, to the other ethyl, alcohol in equal quantity (per kilogramme body-weight of the animal) were given at the same intervals and in the same way. Several different specimens of methyl alcohol were used; these will be described in the proper place.

In the following two experiments the alcohols were given in doses of first six, then of three grammes per kilogramme body-weight; in each case the alcohol was diluted with four times its weight of warm distilled water and introduced into the stomach by means of a tube. The methyl alcohol was a commercial preparation obtained from Eimer and Amend; it was labeled "Methylic Alcohol, Pure," but it yielded a small quantity of iodoform on treatment with iodine and potassium hydroxide; the specific gravity was 0.802 (15.5° C.), which would correspond to about 98 per

cent absolute methyl alcohol, assuming almost nothing but alcohol and water to be present.

IX. Experiment with methyl alcohol, May 21st. Dog, weighing 7.84K.

4.45 p. m., 47G. methyl alcohol diluted with 188G. of water administered.

May 22d, 10 a. m. Animal lying down, unable to get up; conscious. 2.10 p. m., 23.5G. alcohol and 94G. water given. There is a watery discharge from the eyes.

May 23d. The animal is in a deep stupor from which he can, however, be aroused. Is unable to stand. There is a muco-purulent discharge from the eyes.

May 24th. Fibrino-purulent conjunctivitis; cornea hazy. Animal seems unable to see; reacts well to slight noises but shows no reaction when hand is passed before eye.

May 25th. Animal just able to stand; eats a little. Cornea bluish; almost certain that animal does not see.

11.50 a. m., 23.5G. alcohol and 94G. water given. The dog was soon in a deep stupor.

May 26th. Unable to stand; eats nothing; very stupid. Purulent conjunctivitis in one eye; the other eye is not so bad as yesterday.

4.15 p. m., 23.5G. alcohol and 94G. water given.

May 27th. Condition about the same as yesterday but the stupor is greater.

May 28th, 3.35 p. m., 23.5G. alcohol and 94G. water given. At 9.30 p. m. the dog was alive.

May 29th. Found dead at 7 a. m.; has apparently not been dead long. The stomach contained much blood-stained mucus; small ecchymoses were found in the mucous membrane. The urine was strongly reducing towards silver nitrate.

X. Experiment with absolute ethyl alcohol, May 21st. Bitch, weighing 5.02K.

5 p. m., 30.1G. of alcohol diluted with 120G. water administered.

May 22d, 10 a. m. Is able to stand but is somewhat intoxicated.

1.55 p. m., 15.1G. alcohol and 60G. water given.

May 23d. Is able to stand and drinks a little water but refuses food.

May 24th. Lies down most of the time; does not eat. There is no discharge from the eye and the animal undoubtedly sees well.

May 25th. Is standing and seems very bright; eats greedily.

11.40 a. m., 15.1G. alcohol and 60G. water given; animal soon deeply intoxicated.

May 26th. Dog bright; eats a little. 4.10 p. m., 15.1G. alcohol and 60G. water given.

May 28th, 3.30 p. m., 15.1G. alcohol and 60G. water given.

The animal was kept until June 3d, during which time no bad effects whatever were noticed; she ate well and increased in weight to 5.64K.

The following experiments were made in the same way as the above except that the intervals between the doses were somewhat different and different preparations of the alcohols were used. The methyl alcohol was the specimen of Columbian Spirits described above in the description of the experiment on the rabbit (VII); the ethyl alcohol was a 93 per cent solution made by adding distilled water to some commercial absolute alcohol. The effects of these two preparations were compared because Columbian Spirits seems to be used sometimes in place of ordinary grain

alcohol, which usually contains about 93 per cent of absolute ethyl alcohol.

XI. Experiment with Columbian Spirits, May 15th. Bitch, weighing 6K.

5.50 p. m., 36G. Columbian Spirits diluted with 108G. distilled water administered.

May 16th. Animal unable to stand; has diarrhoea with slightly bloody discharges.

4.35 p. m., 18G. Columbian Spirits and 54 G. water given.

May 17th. Lies perfectly still with slow labored respiration; unable to hold head up when aroused.

4 p. m., 18G. Columbian Spirits and 54G. waetr. In a short time animal was in deepest coma; corneal reflex absent.

May 18th, 11 a. m. Completely paralyzed; slight corneal reflex. Has vomited much watery matter and passed soft bad-smelling feces containing blood.

May 19th. Slow, deep respiration; no corneal or other reflexes. Has passed much thin feces containing decomposing blood and with a very disagreeable odor. Was living at 6 p. m.

May 20th. Has evidently been dead many hours.

During the first two days of the experiment there was much lachrymation; before death there was a slightly purulent discharge from the eyes.

XII. Experiment with 93% ethyl alcohol, May 15th. Dog, weighing 10.5K.

6.5 p. m., 63G. of 93% ethyl alcohol diluted with 189G. of water administered.

May 16th. Animal is standing but is intoxicated.

4.40 p. m., 31.5G. alcohol and 94G. water given.

May 17th. Dog standing and is bright and lively; very playful and eats greedily.

3.55 p. m., 31.5G. alcohol and 94G. water given.

May 18th, 11 a. m. Very bright and lively.

May 19th. Seems entirely normal.

The animal was kept 10 days longer; nothing abnormal could be detected and he gained slightly in weight.

In the following experiments the effects of the purest methyl alcohol obtainable (Kahlbaum's "acetone free" methyl alcohol) were compared with those caused by pure absolute ethyl alcohol; the alcohols were given in doses 5G. per kilogramme animal.

XIII. Experiment with pure methyl alcohol, June 5th. Bitch, weighing 6.84K.

2.30 p. m., 34.2G. methyl alcohol diluted with 130G. of water administered.

June 6th. Animal unable to stand but is conscious; does not eat. There are irregular twitchings of the legs. There is a little pus in one eye.

3.20 p. m., 34.2G. of alcohol and 130G. of water given.

June 7th. Lies in a deep stupor; corneal reflex present but very sluggish. Both eyes contain a gelatinous secretion.

2.35 p. m., 34.2G. alcohol and 130G. water given; much of it was vomited soon afterwards.

June 9th. Is conscious but unable to stand; head sways back and forth rhythmically. Both eyes have an extremely viscid purulent discharge which contains a large number of bacteria of various kinds.

2.35 p. m., 34.2G. alcohol and 130G. water given.

June 10th, 8 a. m. Lying in deepest coma; not the slightest reflex of any kind. Much brown, very bad-smelling matter has escaped from the anus. Animal died at 1.35 p. m.

The rugae of the stomach were bright red and bleeding slightly. The intestines, especially in the lower part, were greatly inflamed and showed a number of minute bleeding

points; there were a few ulcers in the rectum. The intestinal contents were of a dirty brown color due to the altered blood and had a very foul odor.

XIV. Experiment with absolute ethyl alcohol, June 5th. Bitch, weighing 7.57 K.

3.15 p. m., 37.9G. ethyl alcohol diluted with 148G. water given.

June 6th. Stands and is very lively; tries to fight with another dog.

3.25 p. m., 37.9G. alcohol and 148G. water given.

June 7th. A little unsteady on its feet but eats and drinks well.

2.45 p. m., 37.9G. alcohol and 148G. water given.

June 9th. Seems entirely normal; bright and active.

2.40 p. m., 37.9G. alcohol and 148G. water given.

June 10th. Slightly intoxicated but eats greedily.

The animal was kept for 14 days and showed no symptoms whatever; her weight increased to 8.5K.

In the following experiment the purest commercial preparation of Columbian Spirits obtainable was given in the same doses (5G. per kilogramme body-weight) as the alcohols in the above experiments. This preparation of Columbian Spirits was perfectly colorless, gave a very slight iodoform reaction; the specific gravity was 0.8 (15.5° C.), which corresponds to a preparation containing slightly more than 98 per cent absolute methyl alcohol and a little less than 2 per cent of water.

XV. Experiment with Columbian Spirits, June 6th. Dog, weighing 6.97K.

3.50 p. m., 34.9G. Columbian Spirits diluted with 132G. water administered.

June 7th. Eats and drinks, but trembles continuously; vomited soon after eating.

2.50 p. m., 34.9G. Columbian Spirits and 132G. water given.

June 9th. Lies in deepest coma; corneal and other reflexes entirely absent; respiration very slow. Occasionally has convulsive movements.

2.30 p. m., 34.9G. Columbian Spirits and 132G. water.

June 10th, 7 a. m. The animal has evidently been dead for many hours. Stomach contained a small amount of altered blood with an extremely foul odor.

In the following experiment the ordinary grain alcohol of commerce (often called "Western alcohol") was used. It contained 92.5 per cent (by volume) of absolute ethyl alcohol. It was given in doses of 6G. per kilogramme body-weight; this corresponds to about 5.3G. absolute ethyl alcohol. Hence the results of this experiment may be compared with those of Experiments XIII and XIV, in which 5G. of absolute methyl or ethyl alcohol were given; the administration of the alcohol was continued longer in this experiment, however.

XVI. Experiment with 92.5% commercial ethyl alcohol, June 19th. Dog, weighing 13.6 K.

2.55 p. m., 81.6G. of alcohol diluted with 245G. water administered. Was soon deeply intoxicated.

June 20th, 7 a. m. Still somewhat intoxicated; eats a little and drinks; vomited later.

1.25 p. m., 81.6G. alcohol and 245 G. water given.

June 21st. Lies down most of the time but is able to stand; eats and drinks a little.

1.10 p. m., 81.6G. alcohol and 245G. water given.

June 22d, 10 a. m. Seems about normal; eats greedily.

June 23d. Seems normal; eats a great deal.

1 p. m., 81.6G. alcohol and 245G. water given.

June 24th. In good condition.

1.45 p. m., 81.6G. alcohol and 245G. water given.

June 25th. Seems to be entirely normal; very hungry.

The animal was kept under observation for 16 days during which time it seemed entirely normal; its weight increased 2.3K.

The results of the above experiment are shown in the following table:

In all of these experiments the dog which received the methyl alcohol died, while those which received equal or larger doses of ethyl alcohol in exactly the same way recovered. The differences between the action of the two alco-

hols, however (and in my experiments this was found to be about 5G. per kilogramme body-weight), the differences between the effects of the two alcohols are just as marked with rabbits as with dogs. I mention these facts for it is possible that experimenters who work only upon rabbits may overlook the difference between the action of the two alcohols unless special attention is given to the dosage.

In the first three experiments rather large doses of the alcohols were given (6G. per kilogramme body-weight). The Columbian Spirits used in the first two experiments was the inferior grade of this preparation already described.

XVII. Experiment with Columbian Spirits, May 15th. Male rabbit, weighing 2.19K.

Date.	Alcohol.	Animal.	Weight of animal.	Quantity of alcohol given.	Dose per K. body weight.	Number of doses.	Result.	Remarks.
IX. May 21st.	"Methylc Alcohol, pure." E. and A.	Dog.	7.84K.	141G. alcohol, 564G. water.	6G. once. 3G. 4 times.	5	Died on 9th day.	Doses given on 1st, 2d, 5th, 6th and 8th days. Distinct changes in the eyes.
X. May 21st.	Absolute ethyl alcohol.	Bitch.	5.02K.	90.5G. alcohol, 360G. water.	6G. once. 3G. 4 times.	5	Survived.	Doses given as in above experiment. During the next week the animal's weight increased to 5.64 K.
XI. May 15th.	Columbian Spirits.	Bitch.	6K.	72G. Col. Spts., 216G. water.	6G. once. 3G. twice.	3	Died on 5th day.	Doses given at intervals of about 24 hours on 3 successive days. Conjunctivitis.
XII. May 15th.	Pure ethyl alcohol, 95%.	Dog.	10.5K.	126G. alcohol, 377G. water.	6G. once. 3G. twice.	3	Survived.	Doses given at intervals of about 24 hours on 3 successive days.
XIII. June 5th.	Kahlbaum's purest acetone free methyl alcohol.	Bitch.	6.84K.	136G. alcohol, 520G. water.	5G.	4	Died on 6th day.	Doses given on 1st, 2d, 3d and 5th days. Purulent conjunctivitis.
XIV. June 5th.	Absolute ethyl alcohol.	Bitch.	7.57K.	151.6G. + 592G. water.	5G.	4	Survived.	Doses given on 1st, 2d, 3d and 5th days.
XV. June 6th.	Highest grade Columbian Spirits.	Dog.	6.97K.	104.7G. + 396G. water.	5G.	3	Died on 5th day.	Doses given on 1st, 2d and 4th days.
XVI. June 19th.	Commercial ethyl alcohol, 95.5%.	Dog.	13.6K.	408G. + 1225G. water.	6G.	5	Survived.	Doses given on 1st, 2d, 3d, 5th and 6th days. During the 16 days following the dog's weight increased to 15.9K.

hols could probably have been brought out still more strikingly if more attention had been given to the dosage.

*Experiments on Rabbits.*—Results in entire accordance with the above were obtained in a series of experiments upon rabbits. These animals are not, however, well adapted for studies on the comparative toxicity of methyl and ethyl alcohols in subacute poisoning, for the doses necessary to cause death within a short time (a few days) vary within narrow limits. The difficulty may be expressed in the following manner: There is a certain optimum dose for subacute poisoning, i. e., a dose with which the difference between the action of the two alcohols is best seen. When the dose of the alcohols is slightly greater than this optimum death is produced almost as rapidly by one alcohol as by the other; when the doses are below this optimum the action is very prolonged and the poisoning takes on a more chronic character. With the optimum

5.25 p. m., 13G. Columbian Spirits diluted with 52G. water administered.

May 16th. Sits in one place and does not try to escape when handled; eats a little.

4.15 p. m., 13G. Columbian Spirits and 52G. water given.

May 17th. Animal comatose; corneal reflex present but very sluggish.

Unnecessary to hold animal when stomach tube was passed.

4.10 p. m., 13G. Columbian Spirits and 52G. water given.

May 18th, 10.45 a. m. The animal has evidently been dead for many hours. The urine reduces silver nitrate very strongly and decolorizes potassium permanganate; does not undergo fermentation with yeast.

XVIII. Experiment with Columbian Spirits, May 19th. Female rabbit, weighing 1.44K.

3 p. m., 8.65G. Columbian Spirits diluted with 34.6G. water administered. An hour afterwards the animal was deeply intoxicated; was unable to hold head up. There was marked nystagmus.

May 20th. Seems to have recovered almost completely.

4.25 p. m., 8.65G. Columbian Spirits and 34.6G. water.

May 21st. Semi-comatose all day; has eaten nothing.  
 4.5 p. m., 8.65G. Columbian Spirits and 34.6G. water given.  
 May 22d. Reflexes entirely absent; seemed barely alive at 6 p. m.  
 May 23d, 7 a. m. Found dead.  
 XIX. Experiment with absolute ethyl alcohol, May 19th. Female rabbit, weighing 1.45K.  
 3.10 p. m., 8.7G. alcohol diluted with 35G. water administered.  
 May 20th. Seems to be entirely normal.  
 4.30 p. m., 8.7G. alcohol and 35G. water given.  
 May 21st. Active; eats well.  
 4.10 p. m., 8.7G. alcohol and 35G. water given.  
 May 22d. Very active; difficult to catch.  
 May 23d. Condition same as that of yesterday; animal eats well.  
 2.30 p. m., 8.7G. alcohol and 46G. water given.  
 May 24th, 9.30 a. m. Very lively. Has aborted two very imperfect embryos.  
 1.45 p. m., 8.7G. alcohol and 46G. water given.  
 May 25th. Seems normal. 11.30, 8.7G. alcohol and 46G. water given.  
 May 26th, 7 a. m. Found dead.

In this experiment the administration of the ethyl alcohol was continued until it caused death—a result which did not occur until just twice the amount (in proportion to the body-weight) which was fatal in the case of Columbian Spirits had been given.

In the following experiment ethyl alcohol of the strength of 93 per cent was given in doses of 6G. per kilogramme.

XX. Experiment with 93% ethyl alcohol, May 15th. Male rabbit, weighing 2.17K.  
 5.35 p. m., 13G. alcohol diluted with 52G. water administered.  
 May 16th. Seems entirely normal; difficult to catch; eats well.  
 4.25 p. m., 13G. alcohol and 52G. water given.  
 May 17th. Seems entirely normal; very lively and difficult to catch.  
 4.5 p. m., 13G. alcohol and 52G. water given.  
 May 18th. Very lively. Weighs 2.05K.  
 The animal was kept for 16 days, during which time it exhibited no symptoms whatever.

In the following experiment ordinary commercial ethyl alcohol (containing about 92.6 per cent of absolute ethyl alcohol) was used; it was given in doses of 6G. each on four days.

XXI. Experiment with commercial ethyl alcohol (92.6%), June 19th. Female rabbit, weighing 1.96K.  
 2.10 p. m., 11.8G. alcohol diluted with 35G. water administered.  
 June 20th. Animal lively; eats a little.  
 2.10 p. m., 11.8G. alcohol and 35G. water given.  
 June 21st. Seems to be in good condition; eats a little.  
 2.25 p. m., 11.8G. alcohol and 35G. water given.  
 June 23d, 3 p. m., 11.8G. alcohol and 35G. water given.  
 June 25th. Seems to be normal.  
 The animal was kept for 16 days during which time it remained in good condition, its weight remained about the same.

The doses in the above two experiments (6G. of the 93 per cent (by volume) alcohol) corresponded to about 5.4G. pure absolute alcohol, hence the results may be compared with those of the following experiment in which doses of 5.5G. of Kahlbaum's purest methyl alcohol were given.

XXII. Experiment with Kahlbaum's purest methyl alcohol, May 19th. Female rabbit, weighing 2.55K.  
 2.30 p. m., 14G. alcohol diluted with 56G. water administered.  
 May 20th. Eating well.  
 4.17 p. m., 14G. alcohol and 56G. water given.  
 May 21st. Looks sick but has been eating.  
 3.55 p. m., 14G. alcohol and 56G. water given.  
 May 22d, 7 a. m. Found dead.

On comparing this experiment with the two described above (Experiments XVII and XVIII) it is seen that the purest methyl alcohol obtainable is about as toxic as the commercial preparation of Columbian Spirits; in fact, death was caused more rapidly by a slightly smaller dose of the former.

The difference between the effects of ethyl and methyl alcohols is well brought out in the following four experiments: the doses used in these experiments (4 to 5 grammes per kilogramme) seem to be those best adapted for causing subacute poisoning in rabbits. The methyl alcohol used in the first experiment was "Kahlbaum's Methyl Alcohol;" it was not the purest specimen prepared by Kahlbaum and gave a slight iodoform reaction; the specific gravity, however, was 0.796 (15.5° C.), which corresponds to a strength of 99.5 per cent. The methyl alcohol used in the third experiment was Kahlbaum's purest methyl alcohol.

XXIII. Experiment with Kahlbaum's methyl alcohol, June 3d. Female rabbit, weighing 1.98K.  
 3.15 p. m., 7.9G. (i. e. 4G. per kilo) diluted with 30.3G. water administered.  
 June 4th. Seems entirely normal.  
 12.25 p. m., 7.9G. alcohol and 30.3G. water given.  
 June 5th. Very lively; eats well.  
 2.25 p. m., 7.9G. alcohol and 30.3G. water given.  
 June 6th, 3.10 p. m., 9.9G. alcohol (i. e. 5G. per kilo) and 37G. water given.  
 June 7th. Lies down most of the time but eats.  
 2.30 p. m., 9.9G. alcohol and 37G. water given.  
 June 9th. Weak and sluggish; does not eat well.  
 2.40 p. m., 9.9G. alcohol and 37G. water given.  
 June 10th. Unable to stand; does not eat.  
 2 p. m., 9.9G. alcohol and 37G. water given.  
 June 11th. Died about 8 a. m.  
 XXIV. Experiment with absolute ethyl alcohol, June 3d. Female rabbit, weighing 1.93K.  
 3.10 p. m. 7.8G. alcohol (i. e. 4G. per kilo) diluted with 30.3G. water administered.  
 June 4th. Seems entirely normal.  
 12.20 p. m., 7.8G. alcohol and 30.3G. water given.  
 June 5th. Very lively; eats well.  
 2.50 p. m., 7.8G. alcohol and 30.3G. water given.  
 June 6th. Same condition as yesterday.  
 3.5 p. m., 9.75G. alcohol (i. e. 5G. per kilo) and 37G. water given.  
 June 7th. Lying down most of the time but eats well.  
 2.25 p. m., 9.75G. alcohol and 37G. water given.  
 June 9th. Seems entirely normal; is quite lively. Eats well.  
 2.20 p. m., 9.75G. alcohol and 37G. water given.  
 June 10th, 1.55 p. m., 9.75G. alcohol and 37G. water given.  
 June 11th. The animal seems to be entirely normal; is quite lively and eats well. Nothing unusual was noticed about it but on the morning of June 14th it was found dead. On autopsy

a smooth typical gastric ulcer was found and bloody peritonitis.

XXV. Experiment with Kahlbaum's purest methyl alcohol, May 19th. Female rabbit, weighing 2.49K.

2.10 p. m., 11.2G. alcohol (i. e. 4.5G. per kilo) diluted with 44.8G. water administered.

May 20th, 7 a. m. Seemed entirely normal. At about 11.30 a. m. aborted 6 embryos; a little hemorrhage.

4.10 p. m., 11.2G. alcohol and 44.8G. water given.

May 21st. Looks sick but has been eating a little.

3.45 p. m., 11.2G. alcohol and 44.8G. water given.

May 22d. Seems completely paralyzed; unable to hold head up.

May 23d. Seems somewhat better but is unable to crawl or to sit.

2.57 p. m., 5.6G. alcohol (i. e. 2.25G. per kilo) and 22.5G. water given.

May 24th. Almost completely paralyzed; slight reflexes.

2.5 p. m., 5.6G. alcohol and 22.5G. water given.

May 25th. Seemed barely alive at noon.

May 26th, 7 a. m. Found dead.

XXVI. Experiment with absolute ethyl alcohol, May 19th. Female rabbit, weighing 2.4K.

2.20 p. m., 10.8G. alcohol (i. e. 4.5G. per kilo) diluted with 43G. water administered.

May 20th. 10.8G. alcohol and 43G. water given.

May 21st. Movements somewhat uncoordinated in the morning but animal eats well.

3.50 p. m., 10.8G. alcohol and 43G. water given.

May 22d. Very lively; apparently unaffected.

May 23d. Seems to be entirely normal.

3 p. m., 5.4G. alcohol (i. e. 2.25G. per kilo) and 21.5G. water given.

May 24th. Animal lively; eats well.

2 p. m., 5.4G. alcohol and 21.5G. water.

May 25th. Seemed entirely normal at noon.

May 26th. Animal seems entirely normal; eats well.

The animal was kept for 13 days longer during which no symptoms whatever could be observed.

The following two experiments in which small doses of methyl alcohol were given for several days may be quoted although the results can scarcely be included under the subject of subacute poisoning.

XXVII. Experiment with Columbian Spirits, May 23d. Male rabbit, weighing 1.96K. This rabbit was given 4.9G. Columbian Spirits (i. e. 2.5G. per Kilogramme) diluted with 24.8G. water daily for 8 days. The animal was slightly intoxicated a number of times but seemed to remain in fair condition although its weight decreased by 300G. 8 days after the administration of the last dose the animal was found dead.

XXVIII. Experiment with pure methyl alcohol, May 23d. Female rabbit, weighing 1.52K. This rabbit received 4.6G. methyl alcohol (i. e. 3G. per kilogramme) diluted with 22.4G. water daily for 8 days. The animal was slightly intoxicated a number of times but showed no marked symptoms; its weight decreased to 1370G. The animal was kept for 20 days without any symptoms being noticed.

The results of the above experiments are shown in the table on opposite page:

The results of these experiments upon rabbits agree entirely with those obtained in the experiments upon dogs and show how toxic methyl alcohol is when its adminis-

tration, in suitable doses, is continued for even a few days. The great difference between the toxicity of methyl and ethyl alcohols might be overlooked entirely in experiments in which only the effects of single large doses were studied.

*Fate of Methyl Alcohol in the Body.*—The explanation of the difference between the toxicity of methyl and ethyl alcohols in subacute and chronic poisoning is to be found in the work of Pohl and others upon the fate of methyl alcohol in the body. The interesting and highly important discovery has been made that methyl alcohol differs markedly from ethyl alcohol (and apparently from the other alcohols of this series) in that it is but partially oxidized in the body and that its administration leads to the formation within the body of a markedly poisonous acid (formic acid). It has been shown by numerous investigators that ethyl alcohol is largely oxidized in the body to water and carbon dioxide, i. e., to harmless products, and Pohl found that not even a trace of an acid formed by its oxidation could be detected in the urine. On the other hand, when methyl alcohol is given to an animal, or to man, a considerable quantity of formic acid can always be found in the urine. The formic acid is excreted very slowly; thus in one of Pohl's experiments 60 ccm. of methyl alcohol were given to a dog by the stomach and the maximum amount of formic acid did not appear in the urine until the fourth day and there was an abnormal amount present three days later. In another experiment the methyl alcohol was injected into a vein and the maximum amount of formates in the urine were not found until the fourth day and two days later they were still present to the extent of 0.42G. Even when small quantities of methyl alcohol are administered (quantities too small even to cause narcosis), formic acid is still found in the urine; this shows how difficult it is for the body to completely oxidize methyl alcohol.

Pohl found a close parallelism between the intensity of the intoxication and the excretion of formic acid; just as the former gradually increased and then decreased so did the amount of formic acid found in the urine.

In my own experiments I frequently tested the urine of animals poisoned by methyl alcohol for formic acid. I found that the urine of such animals decolorized potassium permanganate and was strongly reducing towards silver nitrate, but that it did not undergo fermentation with yeast.

In this formation of formic acid from methyl alcohol we have an interesting illustration of the fact that at times the body converts one poison into another of greater power; this fact is evident when the toxicity of sodium formate is compared with that of methyl alcohol. Mayer (Archiv f. experim. Path. u. Pharm., 21, p. 122) found that 2.5G. of sodium formate injected into the vein of a rabbit weighing 2 kilogrammes caused death in one hour and ten minutes, i. e., 1.25G. per kilogramme is fatal to rabbits. Now, as was pointed out above, Joffroy and Serveaux found that it required about 7.96G. of methyl alcohol per kilogramme

body-weight to cause death; in other words, formic acid is about six times as poisonous as methyl alcohol.

The extent to which the methyl alcohol is converted into formic acid is not known; Pohl obtained 4.58G. of formates from the urine after the intravenous injection of 20 c.cm. of methyl alcohol and the experiment was discontinued when the excretion of formates was still very large (0.42G. on the last day). Pohl thought it probable that all the

oxidation products are eliminated.<sup>1</sup> The slow excretion of the formic acid has already been noted; Pohl showed that this was apparently not due to a retention of the acid in the body, for the intravenous injection of a large quantity of sodium chloride (by which great diuresis and so a thorough "washing out" of the tissues was brought about) had but little effect upon the course of the formic acid excretion. Pohl also failed to find any excess of formic acid in

Date.	Alcohol used.	Animal used.	Weight of animal.	Amount of alcohol given.	Dose per kilogramme.	Number of doses.	Result.	Remarks.
XVII. May 15.	Columbian Spirits.	Rabbit.	2.19K.	39 G. + 156G. water.	6G.	3	Died on 3d day.	Doses given at intervals of about 24 hours on 3 days in succession.
XVIII. May 19.	Columbian Spirits.	Rabbit.	1.44K.	25.95G. + 103.8G. water.	6G.	3	Died on 4th day.	Doses given at intervals of about 24 hours on 3 days in succession.
XIX. May 19.	Absolute ethyl alcohol.	Rabbit.	1.45K.	52.2G. + 210G. water.	6G.	6	Died on 7th day.	Doses given on 1st, 2nd, 3d, 5th, 6th and 7th days.
XX. May 15.	Ethyl alcohol, 93%.	Rabbit.	2.17K.	39G. + 156G. water.	6G.	3	Survived.	Doses given at intervals of about 24 hours on 3 successive days.
XXI. June 19.	Commercial ethyl alcohol, 92.6%.	Rabbit.	1.96K.	47.2G. + 140G. water.	6G.	4	Survived.	Doses given on 1st, 2nd, 3d and 5th days.
XXII. May 19.	Kahlbaum's purest, acetone free methyl alcohol.	Rabbit.	2.55K.	42G. + 168G. water.	5.5G.	3	Died on 3d day.	Doses given at intervals of about 24 hours on 3 successive days.
XXIII. June 3.	Kahlbaum's methyl alcohol.	Rabbit.	1.98K.	68.3G. + 202G. water.	4G., then 5G.	7	Died on 9th day.	Doses given on 1st, 2nd, 3d, 4th, 5th, 7th and 8th days.
XXIV. June 3.	Absolute ethyl alcohol.	Rabbit.	1.95K.	62.4G. + 202G. water.	4G., then 5G.	7	Died from peritonitis caused by gastric ulcer.	Doses given on 1st, 2nd, 3d, 4th, 5th, 7th and 8th days.
XXV. May 19.	Kahlbaum's purest, acetone free methyl alcohol.	Rabbit.	2.49K.	44.8G. + 179.4G. water.	4.5G., then 2.25G.	5	Died on 8th day.	Doses given on 1st, 2nd, 3d, 5th and 6th days.
XXVI. May 19.	Absolute ethyl alcohol.	Rabbit.	2.40K.	43.2G. + 172G. water.	4.5G., then 2.25G.	5	Survived.	Doses given on 1st, 2d, 3d, 5th and 6th days.
XXVII. May 23.	Columbian Spirits.	Rabbit.	1.96K.	39.2G. + 198.4G.	2.5G.	8	Died on 17th day.	Doses given daily the first 8 days.
XXVIII. May 23.	Kahlbaum's purest, acetone free methyl alcohol.	Rabbit.	1.52K.	36.8G. + 179.2G. water.	3G.	8	Survived.	Doses given daily for the first 8 days.

methyl alcohol administered is converted into formic acid and that part of the latter is then oxidized to carbon dioxide. Bongers (Archiv f. exper. Path. u. Pharm., 35, p. 429), on the other hand, asserts that after the administration of methyl alcohol considerable quantities of it are excreted in the urine; if this is the case we have further evidence of the difficulty with which the body oxidizes methyl alcohol. After even large doses of ethyl alcohol only mere traces of it can be found in the urine.

The long continued effects of methyl alcohol in acute poisoning and the ease with which a condition of chronic poisoning is produced by small, repeated doses doubtlessly depends upon the slowness with which the poison and its

the various organs. These observations of Pohl made it probable that either methyl alcohol itself or some derivative of it is retained in the body and is then slowly converted into formic acid. The later observations of Bongers have shown that methyl alcohol itself is retained in the body for some time. This author made the interesting observation that when methyl alcohol was given by the rectum some of it (as well as some formic acid) was excreted into the stomach and that this excretion did not reach its maxi-

<sup>1</sup>This is probably the cause of the blindness which so frequently follows methyl alcohol poisoning in man; highly differentiated nerve structures (such as those of the retina) are especially likely to suffer when exposed to the action of a poison for some time.

num for 21 to 28 hours. These experiments of Bongers are of interest in another connection. The methyl alcohol excreted into the stomach is presumably reabsorbed, either from the stomach or from the intestine, and some of it again excreted into the stomach, so that there is a "circulation" of methyl alcohol just as there is of the bile salts and of morphine; the result is that the irritant action of the methyl alcohol upon the digestive tract is exerted time after time. Now one of the most marked symptoms of methyl alcohol poisoning is great irritation of the alimentary tract; it is probable that this is due in part to the above mentioned peculiarity of the excretion of the drug.<sup>3</sup>

From chemical grounds it seems very probable that formaldehyde is formed as an intermediate product in the conversion, within the body, of methyl alcohol into formic acid. It is true that Pohl failed to find support for the view that any "considerable quantities" of formaldehyde are formed, but it may be that formaldehyde is formed and that it is then quickly converted into formic acid; Pohl himself showed that formaldehyde when administered to an animal is converted into formic acid. If it is supposed that some formaldehyde is formed then we would have another factor in explaining the toxicity of methyl alcohol, for Aronsohn (Berl. klin. Woch., 1892, p. 751) found that 0.24G. of formaldehyde per kilogramme body-weight is fatal to rabbits; in other words, part of the methyl alcohol would be converted into a substance about thirty-three times more poisonous.

Before leaving the subject of the formation of formic acid from methyl alcohol an interesting observation of Pohl's may be mentioned. Pohl showed that the administration of sodium bisulphite simultaneously with the methyl alcohol caused a great increase in the excretion of formic acid in the urine; it would be an interesting problem to determine whether this salt would be of any therapeutic value in cases of poisoning by methyl alcohol.

Finally attention should be called to the fact that Pohl found that methyl alcohol underwent the same change in the human body as in that of the lower animals; its administration to man led to the appearance of formic acid, which was slowly excreted in the urine.

A few words may be said in conclusion upon the subject of the toxicity of the by-products or impurities of methyl alcohol. There is a tendency, especially prevalent among chemists, to attribute the poisonous properties of many substances to the presence of "impurities." Thus it is not so very long since it was taught that the accidents attributed to chloroform were due largely to the impurities present; now it is known that these play but a small part in such accidents. There is still a widespread

belief that the impurities (fusel oil, furfurol, etc.) found in most alcoholic drinks are very important factors in the toxic action of such drinks. Some of these impurities are very much more poisonous than equal quantities of ethyl alcohol, but it has been shown time and time again that they are present in even the worst grades of liquors to such a small per cent that a person would have to consume an amount of the liquor containing many times the fatal dose of ethyl alcohol in order to get a fatal dose of these impurities. The latter undoubtedly somewhat increase the toxicity of the liquor, i. e., a slightly smaller quantity of a liquor containing them would prove fatal than would an equal quantity of pure ethyl alcohol diluted to the same extent, and they may further cause some especially severe symptoms (severe headaches, etc.), but the fact remains (undisputed by competent investigators) that in such liquors the toxic principle par excellence is ethyl alcohol.

It was only to be expected that views similar to the above would be expressed regarding the toxicity of methyl alcohol; in fact, the statement is made in a leading English work on organic analysis that methyl alcohol when free of impurities is not deleterious! Most of the experiments quoted above were made with pure methyl alcohol or with preparations of methyl alcohol so nearly pure that it may be safely assumed that the traces of impurities had no essential influence upon the course of the intoxication. It is undeniable that in some of the crude commercial preparations of "wood alcohol" certain impurities are present in large amount and that the toxicity of such preparations is increased by their presence. It would lead us too far to consider this subject here in detail, but it may be said that the toxicity of these impurities has been tested and that it is doubtful whether in the most impure preparations the impurities are present in sufficient quantity to cause death; in other words, while the toxicity of the preparation may be considerably increased by them, methyl alcohol is still the chief toxic agent. The experiments of Dujardin-Beaumetz and Audigé are of interest in this connection; these authors working as long ago as 1876 found the fatal dose of ordinary commercial wood alcohol to be, for the dog, 5.75G. per kilogramme, while that of pure methyl alcohol was placed by these authors at 7G. per kilogramme.

In this connection the conclusion of Kuhn (Zeitsch. f. Augenheilkunde, 1, p. 42) relative to two cases of wood alcohol poisoning, in one of which blindness, in the other, death had occurred, may be quoted; this author was considering the question whether the symptoms could have been due to the impurities in the wood alcohol; he says that assuming the wood alcohol in question to have been of the most impure variety (one containing even 20 per cent of acetone), it was certain that the symptoms could not have been caused by any of the impurities or by all combined and that they were due to the methyl alcohol and to the methyl alcohol alone.

These experiments on the physiological action of methyl

<sup>3</sup> It would be very interesting to determine whether any formic acid or methyl alcohol is excreted in the tears; the irritation of the conjunctiva noted in my experiments upon dogs suggest such a possibility. Holden also speaks of signs of irritation of the eye in a dog after the administration of methyl alcohol.

alcohol and its fate in the body show conclusively that, however pure the preparation may be, it is totally unfit for use as a substitute for grain alcohol in any preparation which is to be taken internally and especially in preparations which are to be taken for any length of time; this was the conclusion drawn by pharmacologists years ago

from Pohl's work and the sad results which have recently followed the consumption of preparations containing methyl alcohol show the danger of departing from the recognized methods of pharmacy in the manufacture of compounds without full knowledge of the physiological action of the ingredients.

### NOTES ON NEW BOOKS.

*The Principles of Hygiene.* By D. H. BERGEE, A. M., M. D., First Assistant, Laboratory of Hygiene, University of Pennsylvania. (Philadelphia and London: W. B. Saunders & Co., 1901.)

This book is written for physicians, medical students, and others who desire to acquire a broad, modern view of the principles of so important a subject as hygiene.

As stated by the author in the preface, "no attempt has been made to treat the subject in an exhaustive manner," and in consequence a rather general tone of brevity pervades the whole; yet the wide extent of the subject has been admirably focussed and its chief points properly accentuated, so that in spite of condensation the general presentation is not too narrow to mar the usefulness of the work.

The contents being most suitably divided, the sequence of subjects and ideas flow along smoothly, permitting of a ready and thorough understanding upon the part of the reader. The separate consideration of the hygiene of the person, the school, the factory, the army, and navy, and also of marine and land quarantine, give added emphasis to the peculiar adaptations of the science required under such special conditions.

The typography, illustrations and general make-up of the book are of a pleasing and excellent order.

*Eczema.* By L. DUNCAN BULKLEY, M. D. Third edition, 16 mo. (New York: G. P. Putnam's Sons, 1901.)

This manual contains very many valuable points both in the treatment and diagnosis of Eczema, which should be of great value to the student and physician.

From an abundance of clinical material the author has compiled several interesting tables, relative to the age at which the disease appears, its duration and the hereditary distribution.

We cannot agree, however, with the author in the highly important rôle he ascribes to constitutional diseases in the etiology of eczema. It would seem, from the suspiciously long list of causes of eczema the author gives, that in his zeal to refer all cases to some constitutional origin, he seizes upon any associated condition, no matter how obscure its relation, and magnifies it to a causative effect.

*Bacteriological Diagnosis for Practitioners.* By W. D'ESTE EMERY, M. D., B. Sc., Lond. (Philadelphia: P. Blakiston's Son & Co., 1902.)

The aim of the author is evidently one to enable the busy practitioner to acquire a practical bacteriological training from a perusal of his book, in lieu of a course in the laboratory when such cannot be conveniently undertaken. No matter how carefully and explicitly written such a work may be, and certainly little fault can be found with the author's attempt, it usually fails in its object, because the confidence and feeling of certainty bred of intimate personal contact and demonstration in the laboratory, can never be attained from mere book study of the subject of bacteriology, especially when the student is burdened with the cares of a medical practice. Therefore, from our point of view, the usefulness of such a book is greatly limited.

*Clinical Hematology.* A Practical Guide to the Examination of the Blood with reference to Diagnosis. By JOHN C. DA COSTA, JR., M. D., Assistant Demonstrator of Clinical Medicine, Jefferson Medical College, etc. Octavo, 474 pages, with eight full-page colored plates, three charts, and forty-eight other illustrations. (Philadelphia: P. Blakiston's Son & Co., 1902.)

The American profession is certainly now well supplied with text books on the blood. This, the latest, promised well, yet we fail to find that it has added anything to our knowledge of the subject, either in original work or in rendering the vast amount of original research any more available to the student. Prolix the book certainly is, and were its contents to occupy half the number of pages little would be lost. The book is excellent for one not particularly interested or especially trained in hematology who wishes to learn what the present status of our knowledge is on some points, or what theory in the author's opinion was best sustained by evidence on the day he wrote that chapter, on other points. It gives a general review, in other words, of the literature for the general medical reader.

The student desiring information on a particular point will often be compelled to search elsewhere. He will find the section on Blood Examination good and Sections II, III and IV, unsatisfactory. He will encounter an indefiniteness of statement like the following, "some observers hold," "it is said," "the old belief," "most authorities" often without any name or reference. "A minimal amount of theoretical discussion" was promised. The author instead states his opinion deduced from studying the data, but gives neither the data nor the references in some cases.

The sections on blood diseases and the blood in various diseases are much better. In these the student can learn more of the work and opinions of different authorities. The author, as do so many, groups the results of his blood observations into tables, adds the figures together and reckons the average. This for all biological reactions as leucocytosis, for example, is of little value and misleading. If we do not know the day of the disease, the temperature, something of the results of the physical examination, and the general condition of the patient we care nothing what the leucocytes are. One case with these points briefly stated and three counts at various intervals (in appendicitis, suspected perforation in typhoid fever, in pneumonia, etc.) will tell more than a table of a dozen cases and an average.

*The American Year-Book of Medicine and Surgery.* Edited by GEORGE M. GOULD, M. D. Medicine. (Philadelphia and London: W. B. Saunders & Co., 1902.)

In noticing the volume on medicine of the year-book for 1902, there is little to be said in addition to the reviews of the volumes of previous years. The work maintains its high standard, which is no doubt partly aided by the permanence of the editorial staff. We can only repeat the favorable opinion previously expressed.

A Laboratory Course in Bacteriology. By FREDERIC P. GORHAM, A. M., Associate Professor of Biology, Brown University. (Philadelphia and London: W. B. Saunders & Co., 1901.)

There seems to be little else presented in this book than can be found in most of the recent text-books upon the subject. And in consequence it seems difficult to divine any advantage that can be gained by its employment, inasmuch as in all well-appointed laboratories the class demonstrations serve to amplify and accentuate the text-book in such a manner that the necessity for so brief an exposition of the subject as presented in the author's work seems superfluous.

Diseases of the Intestines. Their Special Pathology, Diagnosis and Treatment. Vol. II. By JOHN C. HEMMETER, M. D., Philos. D., Professor in the Medical Department of the University of Maryland, etc. Octavo, 675 pages, with plates and many other illustrations. Price, Vol. II, net, \$5.00. Set complete, \$10.00. (Philadelphia: P. Blakiston's Son & Co., 1902.)

This volume is largely the work of the author himself, fewer writers having collaborated with him than was the case with volume I. The section on Diseases of the Rectum was written by Dr. Thos. Chas. Martin, Professor of Proctology in the Cleveland College of Physicians and Surgeons.

The writer first takes up the consideration of appendicitis, with its pathology, symptomatology, treatment, etc. We are glad to see that he advocates more strongly than he formerly did the use of the knife in the treatment of this disease. When, however, an author continues to make the statement that "Operation should be considered when the signs and symptoms enumerated indicate a suppuration," we feel that he has not yet fully realized the necessity of early operation in this affection. We believe that suppuration should not be waited for, but that the appendix should be removed as soon as possible after a definite diagnosis of appendicitis has been made.

Other chapters are devoted to Tuberculosis, Syphilis, Actinomycosis of the Intestines, the Occlusions, Contusions, Rupture, Enterorrhagia, Intestinal Surgery, Atrophy, Abnormalities of Form and Position, Thrombosis, Embolism, Amyloidosis, Neuroses of the Intestines, Intestinal Parasites and Diseases of the Rectum. The various diseases are on the whole well treated.

Considering that the author has written two large volumes on Intestinal Diseases, we think that relatively too little space has been given to the chapter on Parasites of the Intestinal Canal. Throughout the volume the word "*tubercular*" is used when "*tuberculous*" is meant and is the better term. Many conditions may be tubercular but only a portion of them may be tuberculous.

The two volumes will no doubt be of service to practitioners for purposes of reference. Probably the most serious fault they possess is the lack of brevity and conciseness so necessary in these days when nearly everyone who attains to a professional chair feels it his duty to write a text-book or series of text-books on his specialty.

Lectures on Chemical Pathology in its Relation to Practical Medicine. By C. A. HERTER, M. D., Professor of Pathological Chemistry, University and Bellevue Medical School, New York. (Philadelphia: Lea Brothers & Co., 1902.)

The reputation of the author as an investigator of years standing along the lines of physiological chemistry and chemical pathology should be sufficient assurance of the excellence of a book bearing the above title. A careful study of it amply supports these anticipations.

The book is based on lectures which were delivered by the

author at the University and Bellevue Hospital Medical College during the sessions of 1899-1900 and 1900-1901.

The lectures are eminently practical. A great variety of subjects is dealt with in a most attractive manner. The volume is not a description of the normal physiological processes going on in the healthy body but rather an account of the altered chemical changes which take place in the different organs and secretions in various diseases. The book is full of interesting practical points, and we consider those students most fortunate who have had the opportunity of listening to these lectures.

The volume contains 461 pages. The first chapter is devoted to an interesting consideration of "The Chemical Defences of the Organism against Disease." The bactericidal action of the various fluids and secretions is discussed. The question of the production of immunity is presented in a very clear manner and is brought up to date by the incorporation of Ehrlich's interesting side-chain theory. Among the more interesting chapters are those treating of the abnormal metabolism of the proteids, carbohydrates and fats. Another is devoted to a discussion of the causes and results of excessive gastro-intestinal fermentation. The section describing the metabolic changes present in diabetes is particularly valuable. The concluding chapter is given to a consideration of the disturbances of the body functions occurring in starvation, under-nutrition and obesity.

We can highly recommend the volume to both students and physicians. With a thorough knowledge of its contents a practitioner will be far better equipped to treat his patients intelligently.

A Practical Treatise on Diseases of the Skin. By JOHN V. SHOEMAKER, M. D. Fourth edition, 8vo. (New York: D. Appleton & Co., 1901.)

A striking feature, of this 4th edition of the author's work, is the immense space he has devoted to the treatment of skin diseases. Over 165 pages have been covered in the discussion of general therapeutics and formulary, besides the space given to the special methods of treatment of each disease. No mention is made of the value of light rays.

It is unfortunate that the author, having spent so much time on this one feature, did not devote a little more to the diseases themselves, for, in the table of contents, quite a number of names are omitted, and in the body of the book the description of others is not complete.

The illustrations are good, especially the twelve full-page chromogravure plates, which are well selected.

A Manual of Clinical Diagnosis, by means of Microscopical and Chemical Methods, for Students, Hospital Physicians, and Practitioners. By CHARLES E. SIMON, M. D. Fourth edition, thoroughly revised. Octavo, illustrated with 139 engravings and 19 plates in colors. (Philadelphia and New York: Lea Brothers & Co., 1902.)

This is a revised and enlarged edition. This work remains the most comprehensive book in English, covering as it does the whole field of clinical microscopy and clinical chemistry, yet it is well arranged, convenient to use, and thoroughly to be recommended to any student who desires but one book for these subjects.

A Text-Book of Physiological Chemistry for Students of Medicine and Physicians. By CHARLES E. SIMON, M. D., of Baltimore, Md. (Philadelphia and New York: Lea Brothers & Co., 1901.)

The importance of a thorough knowledge of the chemical processes going on in the human body under physiological con-

ditions cannot be over-estimated. Such knowledge is very essential, owing to the fact that in nearly every morbid process the metabolic functions are in some way or other disturbed. It is therefore important that the student and practitioner should have a convenient text-book on physiological chemistry at their disposal. Simon has apparently succeeded in presenting in a concise way the essentials which underlie our knowledge of chemico-physiological processes. Additional interest is attached to the book in that, so far as the reviewer is aware, it is the first text-book on physiological chemistry written and published in this country.

The work contains 453 pages and at first inspection seems to bristle with formulæ, but this proves to be a pardonable sin as most of them are rather essential to a clear understanding of the chemical processes described.

There are 22 chapters in all. The best general idea of the contents of the book will probably be obtained from an enumeration of the subjects of the various chapters in the order taken up. They are as follows: Introduction; The Albumins; The Carbohydrates; The Fats; The Nitrogenous Derivatives of the Albumins; The Ferments; The Digestive Fluids; The Processes of Digestion and Resorption; Analysis of the Products of Albuminous Digestion; Bacterial Action in the Intestinal Tract; The Feces; The Urine; The Animal Cell; The Blood; The Lymph; The Muscle-Tissue; The Nerve-Tissue; The Eye and the Ear; The Supporting Tissues; The Skin and its Appendages; The Glandular Organs of the Body; The Ductless Glands. The best of these chapters is that devoted to the urine, the author having been personally most interested in the chemistry of this secretion.

Although the book can never supplant such an excellent treatise on the same subject as that of Hammarsten's, yet it will be available to a larger body of students and practitioners in this country owing to the latter work being in German.

**Water and Water Supplies.** By JOHN C. THRESH, D. Sc. (London); M. D. (Victoria); Lecturer on Public Health, London Hospital Medical College, etc. Third edition, revised and enlarged. 12mo, 527 pages. Price, \$2.00 net. (*Philadelphia: P. Blakiston's Son & Co., 1901.*)

This very interesting little book was written not for the specialist in Hygiene, but for "all persons interested in public health"; hence it is not a "treatise on Engineering" nor is it a reference or text-book which would aid a person desiring to learn how to make a chemical or bacteriological examination of a water supply. It does, however, tell in a very thorough and interesting manner what has been learned and accomplished by the application of these sciences to water and the water supplies of many countries, and is a book strongly to be recommended to all citizens "interested in public health" for their instruction, and to all not interested for their enlightenment.

**American Edition of Nothnagel's Encyclopedia.** Variola, Vaccination, Varicella, Cholera, Erysipelas, Whooping Cough, Hay Fever. Edited by Sir JOHN W. MOORE, of Dublin. (*Philadelphia and London: W. B. Saunders & Co., 1902.*)

This is the second volume of the American edition of Nothnagel's Encyclopedia and the articles are contributed by various authors. Dr. H. Immermann of Basle writes on Variola and Vaccination. The section on Variola opens with a short historical account of the disease. The etiology is fully discussed and the more important work in the parasitology is reviewed. The writer takes a noncommittal stand in regard to possible etiological organisms. In considering the symptoms the view is taken that those of the initial stage are more

characteristic than the eruption itself. The eruption may vary but the illness of onset is very constant. A mild onset indicates with certainty a mild subsequent course but from a severe onset no conclusion can be drawn. The initial rashes are well described under the headings of "measles-like" and "scarlatinous." The former is considered to occur almost exclusively in cases of varioloid. In reference to the rash of variola vera one point is brought out on which the usual descriptions of the disease lay but little emphasis, namely, that the rash comes out gradually on different parts of the body and that two days may separate the appearance of the rash on the face and on the extremities. The various forms of the disease are fully described and the complications and sequelæ are noticed. The section on diagnosis hardly seems full enough. The impression given is that there is but little difficulty in making the diagnosis. The character of many of the cases on this continent in recent epidemics with the possibility of mistaking them for varicella would lead many to be more cautious than to dismiss lightly the possibility of mistake and especially so when the colored race furnish many of the patients. Under treatment the preference for local applications is given to moist cold. The treatment by red light is alluded to by the editor, but in general but little value is attributed to any means for limiting the amount of scar formation. The author throughout lays emphasis on the "ounce of prevention" in "the careful and most general use of vaccination and revaccination."

The section on vaccination is excellent. If a doubt as to its value has arisen in the minds of any of the profession the reading of this article is strongly recommended. The closing remarks on pages 277-279 should especially be noted. They sum up the whole question of vaccination.

Varicella is discussed by Theodore von Jürgensen of Tübingen. At this day it seems hardly necessary to discuss the question as to the non-identity of variola and varicella. The section on diagnosis is quite inadequate. To state that in any doubtful case if the patient has passed the age of puberty the disease is certainly smallpox, is far from correct. Had this, however, been done always in the United States in the last few years it is fair to say that there would have been fewer smallpox epidemics, but we must remember the occasional occurrence of chickenpox in adults.

Dr. C. Liebermeister of Tübingen writes on Cholera asiatica and nostras. The descriptions are full and the experience of the epidemic of 1892 is fully utilized. Dr. Lenhart of Hamburg discusses Erysipelas. This is a most interesting article. In the section on prophylaxis the question of the necessity of isolation of patients in medical wards is discussed. The writer speaks of the rarity of contagion where there are no wounds. The association between erysipelas and nasal conditions is important in this connection. Under treatment, simple soothing applications are advised. No mention is made of the use of the chloride of iron internally by the author but it is alluded to in a note by the editor, who, however, seems to prefer the administration of quinine and salicylate of sodium alternately.

Whooping-cough is considered by Dr. G. Sticker of Giessen. One naturally turns to the chapter on treatment and this to be appreciated must be read. There is no better discussion of the handling of this disease anywhere. There are so many good points that it is quite impossible to make any selections that would do justice to it. The same writer contributes the last article in the volume on "Bostock's Summer Catarrh," under which designation we find hay-fever is described. The opening sentence of the chapter on treatment may be quoted, "Not one single case of Bostock's catarrh has so far been cured." The various palliative measures are fully discussed.

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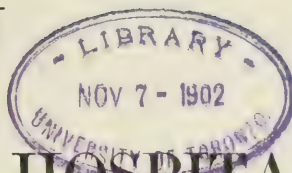
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## THE GENESIS OF GLIOMA RETINÆ IN NEUROGLIA.

By BROWN PUSEY, M. D.,

*Formerly House Surgeon, New York Eye and Ear Infirmary.*

*(From the Pathological Laboratory of Rush Medical College, Chicago.)*

It is commonly accepted by anatomists that the rod and cone cell layer of the retina is made up of highly differentiated cells, and this idea prevails notwithstanding differences of opinion as to their nature. Some authorities (Barker, 1) liken these cells to the so-called neuro-epithelial cells in the taste buds of the tongue; that is, they are thought to be differentiated epithelial cells with which the peripheral fibres

of the bipolar cells come in contact. Another opinion which is based especially on recent work by v. Lenhossék (2) is that these cells are sensory nerve cells.

In any consideration of tumors of the retina one must remember that "Histoid tumors (in which one or other tissue is more or less faithfully reproduced) are essentially benign; and malignancy and excessive cell proliferation

(which is the essence of malignancy) go hand in hand with tumor formation of a pronounced embryonic type" (Adami, 3).

In recent publications Flexner (4) and Wintersteiner (5 and 6) have adopted a different view. By independent investigations they concluded that the most malignant tumors of the retina are composed in large part of these most highly specialized cells. Wintersteiner's (?) description of the rosette figures found in such tumors is as follows: "Alle die Rosetten und bandartigen oder bogenförmigen Zellenformationen als Aggregate von Stäbchen, eventuell Zapfenfasern aufzufassen. Die Zellkerne haben demnach die Bedeutung der Körner in der äusseren Körnerschichte; die glänzende, dem Lumen der Rosette respective der Concavität des Bogens zugewendete Linie entspricht der Membrana limitans externa, die kleinen Protoplasmaklumpchen, welche derselbe anhaften, sind rudimentär entwickelte Stäbchen u. vielleicht auch Zapfen." Flexner's (8) description of the rosette formations is practically the same. From the study of these formations, Wintersteiner has suggested the term *Neuroepithelioma retinae*<sup>1</sup> to replace the term *Glioma retinae*. This suggestion has been the subject of not a little contention. In opposition it is urged that the rod and cone cell layer consists of cells intimately concerned with the visual sense, that, indeed, they are specialized nerve cells of a high order (v. Lenhossék, 9); and the position taken by practically all pathologists that nerve cells do not, at least in post-natal life, proliferate to form tumors.

In referring to primary tumors of the nervous system, writers divide them into those arising from neuroglia and those composed wholly or in part of other elements of the nerve tissues. The latter group includes neuromas, consisting largely of nerve fibres, and gangliomas or neurogangliomas, i. e., tumors composed, at least in part, of nerve cells. Naturally, the questions that have arisen as to the proliferation of nerve cells in tumors have concerned the gangliomas (*Neuroma ganglionare*). Concerning this class of tumors Birch-Hirschfeld (10) has written: "Für das Vorkommen ganglionar Neurome lassen sich nur vereinzelte und zum theil unsichere Beobachtungen aufführen—bei der Heteropie grauer Hirn-substance, welche wiederholt durch den Befund grauer Inseln im Marklage des Gehirns erwiesen wurde, handelt es sich um eine Entwicklungsstörung; der Ausgang wirklicher Geschwülstbildung von solchen Inseln ist nicht nachgewiesen." Gibson and Fleming (11) in Allbutt's System state that: "Ganglion cells have been found in one or two rare cases, but their occurrence is quite exceptional;" in Ziegler (12) we find that "probably all such formations must be regarded as the result of a disturbance of the embryological development of the brain." "In all events, however, the investigations referred to are not sufficient to demonstrate certainly the existence of true neuromas of the spinal cord" (Lubarsch, 13). Casper (14)

states that in animals true neuromas have not been demonstrated with certainty. Klebs (15) dismisses the subject by saying: "Im ganzen ist indess diese gangliöse Umwandlung der proliferierenden Nervenfasern eine Seltenheit und besteht noch seltener ein solcher Tumor überwiegend aus Neugebildeten Ganglionzellen." Thoma (16) notices descriptions of such tumors by Klob, Virchow and Wagner. Orth (17) cites two cases reported by Klebs and Soyka.

From the above quotations we see that Birch-Hirschfeld, Ziegler, Gibson and Fleming, Lubarsch, and Casper deny that tumors of the nervous system occur in which ganglion cells have multiplied to any considerable extent; Klebs finds that such tumors are rare; Thoma refers to three cases published in 1858, 1861 and 1863, and Orth notices reports of two cases.

The absence of evidences of proliferation of nerve cells in tumor growths is in accord with the results of investigations of the behavior of these cells in inflammatory processes. This subject has recently been very thoroughly considered by Tedeschi (18), who reviews the literature and reports experiments of his own; he finds that cicatrices of more or less extensive cerebral wounds consist in greater part of neuroglia, in the centre of which there are a few ganglion cells and a moderate mass of fibres.

In view of the inability of ordinary neurocytes to proliferate either in inflammatory processes or in tumors, it seems unlikely that the visual nerve cells of the retina (accepting the teaching of v. Lenhossék) should have that power.

There are yet other objections to Wintersteiner's views. One is the difficulty in accepting his explanation of the genesis of the rosette in face of the fact that very similar formations occur in gliomas of the central nervous system. Another difficulty is encountered in the wall of the lumen around which the cells are aggregated to form the rosette. He considers this wall to be analogous with the *membrana limitans externa*—a structure which all authorities agree is neuroglia. The lining of the channel in the rosette formations is within a mass of cells and is a part of a mass of cells which according to Wintersteiner and Flexner form embryonic rod and cone cells; it seems hardly probable that such cells should form a structure analogous to neuroglia.

Since Flexner's publications and preceding Wintersteiner's book, there appeared an article by Greef (19). Using the silver method of Golgi-Cajal with tissue from a tumor of the retina, he demonstrated that neuroglia-cells formed the principal part of the tumor. His conclusion was confirmed by Hertel (20).

In view of the conflicting opinions, I think that the publication of the results of the study of a specimen stained by Mallory's (21) neuroglia method may prove of interest.

The patient was referred to Dr. C. D. Wescott by Dr. F. C. Honnold; name, O. H.; girl; age, 4 years and 6 months. The parents are not in vigorous health. The history of the family brings out the facts that three aunts of this child have squinted; the mother squints. The patient's general physique is below par; the child is poorly nourished and

<sup>1</sup> This term was used by Flexner, with a question mark, in his article describing such a tumor published some months before Wintersteiner's first publication on this subject.

very nervous. She has had the usual illnesses of childhood; in the last month has had capillary bronchitis. The eyes have always diverged; the parents have noticed this and also the fact that the child is near-sighted, but they have not noticed any inflammatory symptoms. The left eye became red and painful two or three days ago, when the child was taken to see the family physician, who immediately referred it to Dr. Wescott, to whom I am indebted for the enucleated globe.

V-13-'99. P. C. Left eye: The eye on inspection seems rather smaller than a normal eye; there is lacrymation and double injection; cornea is clear; A. C. shallow; at angle of A. C. iris is in contact with the cornea; A. C. clear; iris adherent to lens and pupil only slightly irregular and dilated by atropin; lens cloudy, and behind it in the vitreous chamber, by oblique illumination, an opaque body is seen. No red reflex. Eye tender. V.=0. T.=—1. Right eye: Highly myopic—at least 8 D. Diagnosis given was guarded, but probably tumor. Ordered hot bathing, atropin and to return frequently for observation. VII-10-'99. There has been less injection, but the condition now is about the same as when first seen. A. C. possibly more shallow. T. sub-normal. V.=0. Probable diagnosis of tumor was made and enucleation was advised. I-10-1900. Parents state that the eye has been quiet, but became red again a few days ago. Again advised enucleation. I-12-1900. Enucleation. I-17-1900. Healing uneventful. III-22-1901. The father writes that the child is in fair health.

The eyeball, measuring 23 mm. sag., 22.5 horiz., 21.5 vertical diameter, was put immediately after enucleation in 4% solution of formalin in water, where it remained for forty-eight hours. Hardening was completed in alcohol. The eye was halved in its antero-posterior diameter, bisecting the optic nerve and cornea. One-half was embedded in celloidin and cut in serial sections. The sections varied from ten to twenty microns in thickness. Every fifth section was stained with hæmatoxylin-eosin; other sections were used for special stains: Mallory's neuroglia, Weigert's neuroglia, Weigert's fibrin and Weigert's elastic tissue stains, and stains for micro-organisms, etc.

*Macroscopical examination.*—It is noteworthy that the eye is undersized. The sclera posteriorly is twice as thick as the normal tissue; A. C. shallow; iris bombé; lens cataractous posteriorly. The retina is detached and appears to be of normal thickness posteriorly, much thickened anteriorly and particularly where it is caught up and attached to the lens. The retina has streaks of pigment in it. The vitreous chamber is clear; the space between the retina and choroid contains some flaky opacities.

*Microscopical examination.*—The tissues of the cornea and sclera are histologically normal. The vessels at the corneal junction are distended. In the anterior chamber along Descemet's membrane, which is normal, there is an albuminous deposit free from cellular elements. At the angle of the anterior chamber the iris is adherent to the posterior surface of the cornea.

The iris shows the changes of an old iritis; it is thinned and made up of fibrous cicatricial tissue. Adhesions exist between the capsule of the lens and iris at its pupillary margin. The ciliary body and ciliary processes show much fibrous cicatricial tissue, and the ciliary body contains an unusual number of pigmented cells.

The lens is cataractous. Under the anterior capsule, where the pupillary margin of the iris has become adherent to it, there are new connective tissue cells, which are mostly spindle shaped. The cortex of the lens is detached from the nucleus in a noticeable degree. The nucleus shows little change. The cells of the cortex show various stages of degeneration, many being swollen and granular, and there are many areas of calcareous deposit. In numerous sections the lens is seen to be invaded by strange cells which are pigmented, have a large granular nucleus, and are identical in appearance with the cells found in the retina. The fibres of the zonula are also infiltrated with similar cells.

The choroid is of normal thickness; its vessels are engorged with blood. At points it is the seat of an infiltration of large mono-nuclear and polymorpho-nuclear cells, a few plasma and mast cells.

The cells of the pigment layer of the retina show a most interesting increase in number. In some places they form rows several cells deep; in other places, considerable masses. One of these accumulations forms a detached mass made up of pigmented cells from the pigment cell layer of the retina. This mass, in cross section in its thickest portion, is about 1 mm. in diameter; it runs through thirty sections, which average in thickness twenty microns. Therefore, it is about 6-10 of a mm. in its other diameter. This mass of cells is detached a little from the choroid, probably caused by shrinkage incident to the hardening. The cells of this mass have no regular shape—they are crowded together. The nuclei are large and granular, and the cell body is of varying size. The amount of pigment also varies.

In the optic nerve the cellular elements predominate over the fibres. These cells have large granular nuclei and but small bodies. There are some leucocytes.

*RETINA.*—Posteriorly the retina is of about normal thickness, except just at the entrance of the optic nerve, where there is an increase of cells and a resulting thickening. Anteriorly there are several regions where the tissue is considerably increased in thickness, and near the ora serrata, in one series of sections, the retina is folded on itself. The lack of resemblance to normal retina is striking, the tissue having a reticular structure in which the fibres greatly predominate. Sections of the posterior part of this tissue, stained with Mallory's neuroglia stain, show that this portion is composed principally of a meshwork of neuroglia fibres. Scattered about are cells with large granular nuclei and unusually small protoplasmic bodies. The fibres are abundant; they extend in all directions. The fibres are long and narrow, and with Mallory's stain they are bluish-black. There are some cells, which have the same large granular nuclei, but more of a protoplasmic body; and some

of these cells contain pigment granules. These latter cells are found particularly along the inner surface of this tissue; in many places lying internal to the internal limiting membrane. The pigment is in granules and is yellowish-brown.

Where the tissue is increased in thickness there is a resemblance to normal retina, and in this region the framework—the neuroglia tissue—takes Mallory's neuroglia stain well, and is seen to be excessive. The internal limiting membrane, or, speaking guardedly, the membrane in which Müller's fibres terminate, appears as a much thickened homogeneous layer (a, Fig. 1). It is interesting to note that this membrane along its retinal surface gives the staining reaction of neuroglia; but in its greater extent along the internal surface it does not stain as such. Internal to the internal limiting membrane and in the cavity of the vitreous there are cells with large nuclei and protoplasmic bodies similar to those described above; and scattered among these cells one finds a few neuroglia fibres (b, Fig. 1). The protoplasm of these cells in places contains pigment-granules. In this region, the fibres of Müller (c, Fig. 1) are increased and abnormally thickened. The most noticeable increase in Müller's fibres is in the region of the internal membrane and the fibres radiate from this region into the deeper layers of the retina. In the part of the retina normally occupied by the internal and external nuclear layers, in this thickened portion, there is a mass of fibres and cells.

Near the ora serrata the tissue is folded on itself, the folding being particularly marked by the thickened internal limiting membrane. In this region the cellular elements predominate. The cells have large granular nuclei, and contain a moderate amount of cytoplasm. They are usually spindle-shaped. Some of the cells contain pigment granules. Interlaced around these cells are long neuroglia fibres, in some places very abundantly. Internal to the internal limiting membrane, and in the cavity of the vitreous, there is marked formation of new cells. In places the internal limiting membrane has been broken through by the cells. Interlaced among the cells are numerous long neuroglia fibres.

Many rosettes are scattered throughout this tissue. The formation of rosettes seems to be due to the tendency of the cells to arrange themselves in rows. In some places the rows are straight, in others, curved and circular, either around a blood vessel or around an empty space.

The rosettes (Fig. 2), as seen in sections stained by hæmatoxylin and eosin, are best described with Fuch's (22) words: The structure "resembles the cross-section of a tubular gland. Surrounding its lumen are long cylindrical cells, whose nuclei lie at their peripheral extremities. The centrally directed extremities are bounded by a clear-cut line. From this latter short conical processes of protoplasm project into the lumen of the gland-like structure."

In sections (Fig. 3) stained with hæmatoxylin-eosin, perivascular rosettes appear to be made up of long cylindrical cells, whose layers of nuclei lie in the peripheral ends of the

cells. The central ends of the cells appear to be lost on the wall of the vessel. The terminal filaments of the cells, ending on the blood vessel, cause the wall of the vessel to appear thickened.

The appearance of both these forms of rosettes, in sections stained with Mallory's neuroglia stain (Fig. 4), is very different from that when stained by hæmatoxylin-eosin. The neuroglia stain (a, Fig. 4) shows the layers of large granular nuclei; and, extending from the region of the nuclei towards the central lumen or vessel, are many long fibres (b, Fig. 4, Fig. 5, Fig. 6), which give the staining reaction of neuroglia. Some of these fibres show an apparent attachment to the cell; others do not show any such intimate relationship. The terminal filaments of the neuroglia fibres, in part, appear to end in and form the wall; other fibres (c, Fig. 4) project into the lumen.

In a careful search through many sections I could find no cells that resembled rod and cone cells; a few large cells were found that might be taken for ganglion cells, such as occur normally in the nerve fibre layer of the retina. The blood vessels are rather plentiful. When terminal filaments of neuroglia fibres form a membrane along a vessel wall, the latter appears much thickened. The membrane is homogeneous and hyalin and does not have the staining reaction of neuroglia. It is an interesting fact that the membrane found around such vessels stains with all stains, as does the membrane corresponding to the internal limiting membrane. There are no signs in the retina of an inflammatory process, except near the optic nerve where there are a few polymorphonuclear leucocytes around the blood vessels.

**CONCLUSION.**—The principal conclusion to be arrived at from the structure of this specimen is that this is a retina in which the neuroglia tissue has been developed at the expense, one may say, of the other tissues. In proof of this are the facts: (a) That the ordinary nervous tissue elements of the retina, the rod and cone cells, the layer of bipolar cells, the ganglion cells, are either absent entirely or present in very scanty numbers. (b) The neuroglia tissue is greatly increased, as shown by Mallory's stain.

Along the inner surface of the internal limiting membrane, and growing through it from the tissue outside, which in this eye represents altered retina, are cells with characteristic large granular nuclei and with varying amounts of cytoplasm, some of them containing pigment, and interlaced among these cells are long neuroglia fibres. In other words, neuroglia tissue has invaded the cavity of the vitreous. That these cells constitute a new growth is plain also from the fact that they have invaded and destroyed the crystalline lens. Composed as it is of neuroglia, the tumor is a glioma.

From the staining reaction with Mallory's neuroglia stain, there seems to be no question of the neuroglial character of the rosettes. And, if these formations are compared with normal retinal tissue, as Flexner (23) and Wintersteiner (24) did, I think it would be more accurate to say that the wall of the lumen of the rosette corresponds to the internal limiting membrane (not the external); the radiating fibres,



FIG. 1.—a. Thickened internal limiting membrane.  
b. Cells and neuroglia fibres internal to internal limiting membrane.  
c. Müller's fibres.

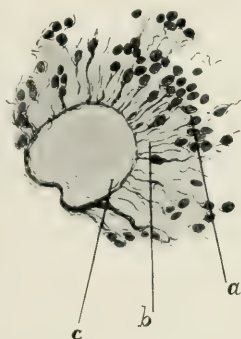


FIG. 4.—Rosette stained with Mallory's neuroglia stain.  
a. Layers of granular nuclei.  
b. Fibres from nuclei to wall of lumen.  
c. Fibres projecting into the lumen.



FIG. 5.—Single fibres taken from the same rosette, represented in Fig. 4.

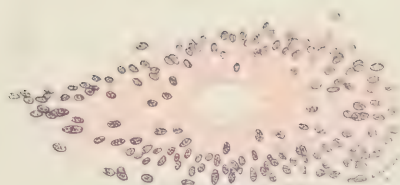


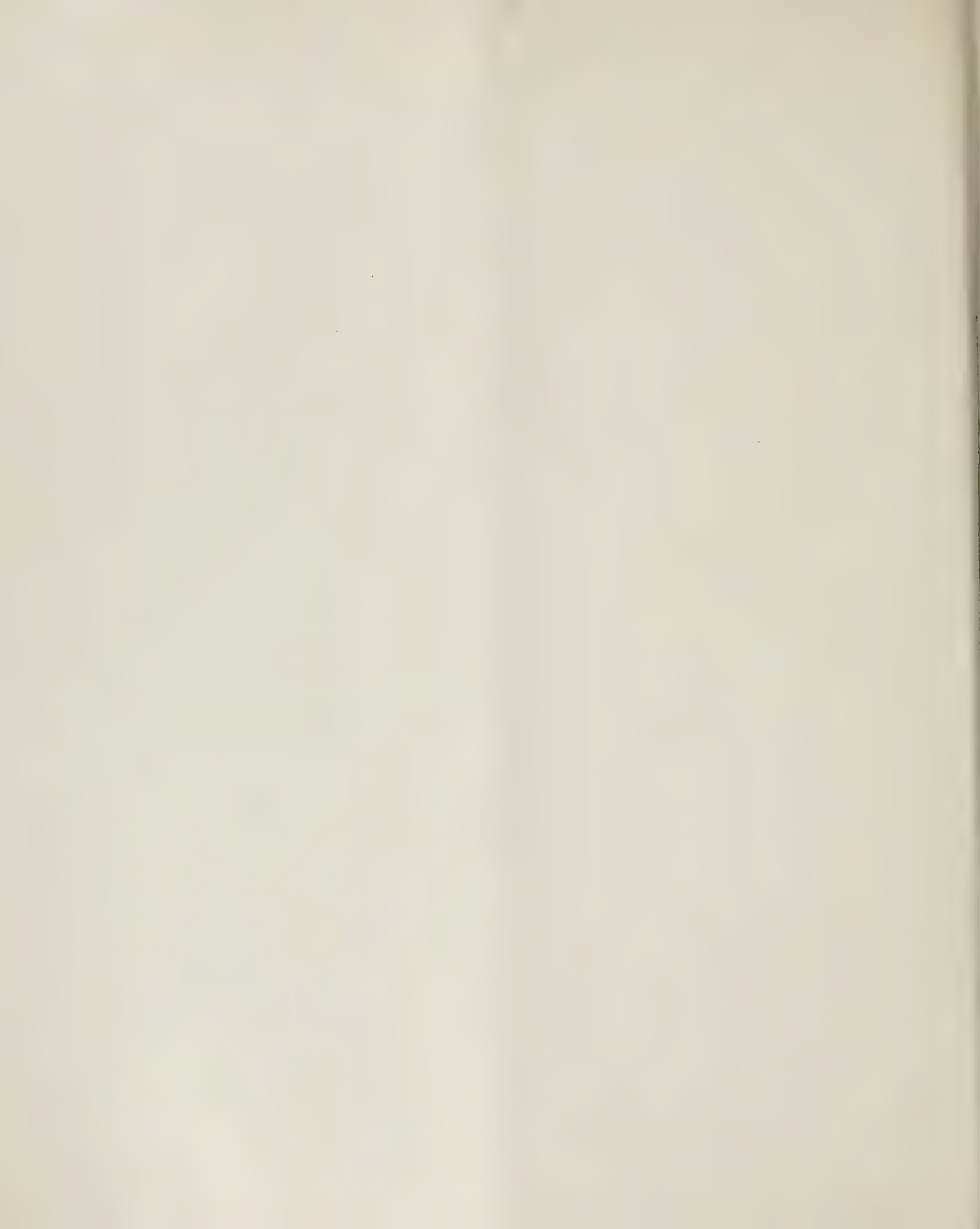
FIG. 2.—Rosette formation stained with hematoxylin-eosin.



FIG. 3.—Perivascular rosette stained with hematoxylin-eosin.



FIG. 6.—Photomicrograph of the same rosette, represented in Fig. 4. (Amplification 1600 dia.)



which are neuroglia fibres, to the fibres of Müller; and the distal nuclei to the neuroglia nuclei normally found in the internal granular layer. The projections into the lumen of the rosette are neuroglia fibres (not rudimentary rods and cones), which have not found their termination in the wall.

The rosettes being composed of neuroglia cells and fibres, the term neuro-epithelioma retinae—as suggested by Flexner and Wintersteiner principally from their conception of the character of the cells in the rosettes—should not be accepted.

The results from the study of this specimen are in accord with what might be expected from a consideration of the facts spoken of in the first part of this paper, and they certainly favor the retention for these retinal tumors of the term first suggested by Virchow and so long accepted—glioma retinae.

There are good reasons for doubting the assertion of Weigert that the neuroglia fibres have no connection with the cell body. In these sections an intimate connection of the fibre with the cell could not always be discerned, but in some areas such a relationship was definitely demonstrated. This agrees with the observation made by Taylor (25), who also used Mallory's stain, and with the conclusion of Bonome (26). The last named author in a recent article states that "A characteristic quality, in which the neuroglia cells more nearly resemble the connective tissue elements, consists not only in the form of the cell body, but also in its relation to the fibrillæ, which in pathological conditions becomes more intimate than in the normal." This latter observation is in accord with Taylor's (27) suggestion of the existence of differentiated and undifferentiated fibres in slowly growing tumors—a suggestion which seems very probable.

In the rosette pictured in figures 4, 5, and 6, it will be noticed that in several fibres there are varicose formations. These are not nuclear figures, as is shown by the fact that the same varicosities are seen in specimens stained with hæmatoxylin and eosin, in which the varicosities show no disposition to take up the hæmatoxylin. Obersteiner (28) noted that changes in neuroglia fibres, of which varicose swelling of the processes is the commonest, may be observed in silver preparations, in alcoholic poisoning, uræmia, and other conditions.

The necrotic changes in glioma of the eye, which take place so frequently in the cells a little removed from the blood vessels, are absent in this specimen. It is interesting to note that this eye was removed before there had been any plus tension in connection with the views of Greef (29), who says that perhaps the peculiar structure of the retinal glioma is dependent on the fact that it is enclosed in the bulbus and that the tension soon becomes abnormally high; growth occurs with difficulty, and, as a result, the cells which do not lie immediately around the scanty vessels die and degenerate.

I did not succeed in staining sections of this tissue with Weigert's neuroglia stain. This was probably due to the manner of preparation of the tissue. Hertel (30) in his case also failed with Weigert's neuroglia stain. Wintersteiner (31) did not attempt to use Weigert's neuroglia method, be-

cause it was not available at the time he carried out his investigations. Recently normal retina has been satisfactorily stained by Weigert's method by Pines (32). In the use of Mallory's neuroglia method, I got the best results by differentiating with an alcoholic solution of ferric chloride after staining; Mallory advises this when good pictures of neuroglia fibres are desired.

The large mass of pigment cells described in the foregoing may be considered as a distinct tumor mass. Axenfeld (33), reviewing the subject of retinal tumors and speaking of the growth of pigment epithelium, cites a case reported by de Vincentis, in which there was a formation of similar cells in a large mass, which was only differentiated from a tumor by degenerative changes. Axenfeld also cites Treacher Collins as having seen gland-like (drüsenartige) growths of the pigment epithelium, resembling a beginning tumor.

I wish to acknowledge my great indebtedness to Professors Hektoen and LeCount for valuable assistance in the preparation of this article.

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## NOTE ON A CASE OF INFECTION BY BACILLUS AEROGENES CAPSULATUS, IN WHICH THE ORGANISM WAS DEMONSTRATED IN THE CIRCULATING BLOOD DURING LIFE.<sup>1</sup>

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The case was that of a young man who was brought into the accident department of the Johns Hopkins Hospital at one o'clock on the night of April 12, in a condition of profound shock. From those who accompanied him it was learned that about two hours before admission he had been struck by a train, which had passed over him, severing both legs. On examination it was found that the right leg had been completely cut across just above the knee and the left leg severed just below the knee, the stumps showing a great deal of laceration and crushing. Tourniquets had been applied to both legs by the doctor who had examined him before admission. The patient had lost very little blood and was not bleeding when examined. His pulse was barely to be felt at the wrist and was uncountable, and he was in a state of such marked collapse that it was considered inadvisable to operate. He was given stimulants and no attempt was made to clean up the injured stumps or to remove the extraneous matter which had been ground into the skin and muscles. Seven hours later his condition had improved sufficiently to justify amputation. The patient, who had retained consciousness, refused, however, to submit to operation, and his friends, all of whom were of a very low, ignorant class, also refused to consent to amputation. Accordingly, the wounds were cleaned as well as possible under the circumstances, and wet bichloride compresses applied. The patient's condition did not improve, his pulse was very

soft and weak, and he failed to rally in spite of marked stimulation.

There was no odor noticed emanating from the stumps until during the night of April 13-14, when the nurse in changing the compresses first detected a foul odor. On the morning of April 14 it was found that both legs up to the thighs were swollen and discolored. The swelling extended to the scrotum, which was several times its normal size. On palpation it was found that the swelling was due to a subcutaneous emphysema, a very definite crepitus being obtained on palpation. Pressure on the scrotum caused the gas to pass up over the groins, when well marked crepitation could be made out over the lower abdomen.

Cover slips made from the stump showed the presence of a large bacillus resembling morphologically *Bacillus aerogenes capsulatus*. Cultures were made from the local seat of infection by Doctor Watts. At 2.30 p. m. I made cultures from the blood of the patient by the following method:

The skin at the bend of the elbow of the left arm was very carefully sterilized. A needle was then introduced into one of the superficial veins and about 8 cc. of blood were withdrawn into a sterile syringe. One cc. of this blood was then introduced into the ear vein of a rabbit. The rabbit was killed after a few minutes had elapsed and was placed in the incubator. The remainder of the blood was divided among 12 tubes of litmus milk. These tubes of milk were then placed in a Novy jar and the air in the jar replaced by hydrogen. The vein was then exposed, a

<sup>1</sup> Presented before the Johns Hopkins Hospital Medical Society, April 21, 1902.

canula was introduced, and 25 cc. of blood were allowed to flow out, being conducted by a rubber tube into a basin of water. The object of this was to determine if possible whether any free gas was present in the circulating blood. No gas bubbles could be observed rising to the surface of the water nor could any gas bubbles be detected in the blood removed in the syringe, so that the presence of free gas was rendered unlikely.

The patient's condition did not improve and he died at 5 p. m., about two hours and a half after the cultures from the blood had been made. The patient retained consciousness up to within an hour of death.

On the following morning the rabbit, which had been allowed to remain in the incubator at 37° C., was found to be distended with gas, and over the abdomen well marked crepitus could be obtained. Autopsy on the rabbit showed the condition of subcutaneous emphysema, gas in the heart and vessels, and other characteristic lesions produced experimentally by *Bacillus aerogenes capsulatus*, as described by Welch and Nuttall. Cover slips made from the liver, spleen, and heart's blood showed the presence of an organism morphologically identical with the above mentioned bacillus. Capsules were demonstrated on the organism on the smears made from the heart's blood. No spores were found.

After growing anaerobically for twenty-four hours the cultures made in milk from the patient's blood were found to have given rise to acidification and coagulation of the milk, the upper surface of the clot showing bubbles of gas. Cover slips made from the milk showed the presence of bacilli resembling *Bacillus aerogenes capsulatus*, in very large numbers. No spores could be demonstrated, even after growing anaerobically for seven days.

The organism obtained in these several ways stained by Gram and was non-motile. In these ways the identity of the organism with that of *Bacillus aerogenes capsulatus* was definitely determined.

The cultures made from the local lesion when grown anaerobically also gave rise to a pure growth of this organism.

Unfortunately, no autopsy could be obtained.

The finding of this organism in the circulating blood during life is of especial interest, in that so far as I can determine, this is the second case in which this has been accomplished. The only other case which is mentioned by Doctor Welch<sup>1</sup> in his review of the "Morbid Conditions Caused by *Bacillus aerogenes capsulatus*," is that reported by Gwyn,<sup>2</sup> in which in a case of chorea insaniens and acute endocarditis he was able on three occasions to demonstrate this organism in the circulating blood of the patient both by cover slip specimens and by cultures, the first culture being made thirteen days before the exitus occurred. This case demonstrated that gas bacilli might be in the circulating blood for days in considerable numbers without evidence of free gas.

The case now reported also demonstrates that whatever the possibility that this organism may produce gas bubbles in the blood during life and that it may produce gaseous emboli, it is quite certain that it may exist in the blood without any, or at least with no considerable, gas production. As Dr. Welch states, this presence of or even multiplication of the gas bacillus in the body during life without the production of gas may occur in other organs and tissues, the demonstration of abscesses without gas having been made by Welch, Cushing, Pratt and Fulton, and Harris.

It is unfortunate that we did not make plates in this case in order to determine the number of organisms in the blood, and so be able to infer whether multiplication had taken place in the circulating blood. It should be mentioned, however, that the tourniquets were constantly applied to the injured legs and not removed at all until after the cultures from the blood had been made, so that there was no possibility of a sudden sweeping of a large number of organisms into the circulation.

<sup>1</sup> Bulletin of the Johns Hopkins Hospital, 1899, x, p. 134.

<sup>2</sup> Bulletin of the Johns Hopkins Hospital, 1900, xi, p. 185.

## AN OBSERVATION SHOWING THAT THE FLAGELLA OF THE MALARIAL PARASITE ARE FERTILIZING ELEMENTS.

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MacCallum, in his studies "On the Hæmatozoan Infection of Birds," *Journal of Experimental Medicine*, Vol. III, 1898, settled a much disputed question regarding the function of the flagella of the malarial parasite.

In his observations upon the Hæmatozoan infection of birds he saw the flagellum from a non-granular body pass over to and penetrate a granular extra-corpusecular body. He had previously observed that only the non-granular bodies

flagellated. This fertilized body soon assumed the fusiform shape of bodies that he had often seen moving about in the field of the microscope.

From what he saw he concluded that these flagella were fertilizing elements and suggested that the same thing would probably be observed in the parasite of the human blood. MacCallum was fortunate in being able to verify his prediction of the occurrence of this phenomenon in the human

blood, for a little later he saw the same process of fertilization take place in the blood from a woman who was suffering from æstivo-autumnal malaria. He states that this process has been observed once by Drs. Warfield and Pancoast of the Johns Hopkins Hospital. Notwithstanding only a few persons have witnessed the process the reliability and accuracy of the observers have not been questioned and the scientific world has generally accepted that the flagella are sexual or fertilizing elements. The observations could hardly be interpreted in any other way.

So far as I can ascertain no other persons than those I have mentioned above have been fortunate enough to witness the flagellum of a non-granular or male form, break away and enter the granular or female form to fertilize it. The rarity of such observation has led me to publish this note.

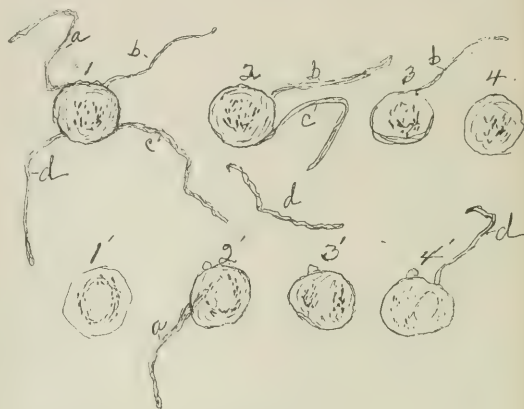
While studying the blood of an æstivo-autumnal fever case to determine whether the flagella were preformed in the body of the malarial parasite I had the good fortune to get both a granular and a non-granular body within the field of the microscope and quite near together.

The pigment of the hyaline body was soon in very active motion, and in a moment four very active flagella were thrust out as shown in Fig. 1. One of these soon freed itself and went plunging around in all directions until it happened to come into contact with the granular body having a wreath-like arrangement of its pigment. After several efforts which I began to fear would be ineffectual the flagellum entered this body. The ring shape of the pigment was soon destroyed, giving the appearance as shown in Fig. 3. About this time another flagellum, *d*, Fig. 1, freed itself and with a movement which seemed purposive and intelligent it struck across the field to the granular body as shown in Fig. 4. Many efforts were made to enter this body but after about five minutes of active effort it wriggled away, apparently abandoning any further effort in this direction.

The other flagella, *b* and *c*, detached themselves and were lost sight of among the red blood cells.

This fertilized body was watched for twenty or thirty minutes, but aside from slight changes in its shape and the distribution of its pigment nothing further was observed to take place.

I have seen in other specimens bodies of a fusiform shape that suggested they might have been fertilized bodies, but in no case did I ever see them swim away as do the vermicules



FIGS. 1, 2, 3 & 4.—Male Flagellating Body.

FIGS. 1', 2', 3' & 4'.—Female Body.

During one-half hour's observation. (Observation, Sept. 10, 1901.)  
Joe Belbo, Sept. 10, 1901.

as observed in the blood of birds and in the mosquito cycle. The body which flagellated soon became inactive and showed evidence of disorganization, while the body into which the flagellum penetrated became slightly swollen but showed no evidence of disintegration. Had it been possible to watch the body longer it might have been seen to pass through the other stages of development.

## GONORRHOEAL ENDOCARDITIS WITH CULTIVATION OF THE SPECIFIC ORGANISM FROM THE BLOOD DURING LIFE.

REPORT OF A CASE, WITH SOME CRITICAL REMARKS UPON GONOCOCCUS SEPTICÆMIA AND THE GONOCOCCUS.<sup>1</sup>

By NORMAN MACLEOD HARRIS, M. B. (TOR.), Associate in Bacteriology in the Johns Hopkins University,

AND

WILLIAM B. JOHNSTON, M. D.,

Late Resident Physician of the Johns Hopkins Hospital in Charge of the Medical Bacteriological Laboratory.

J. A., negro, 20 years old, laborer. Admitted September 18, 1901.

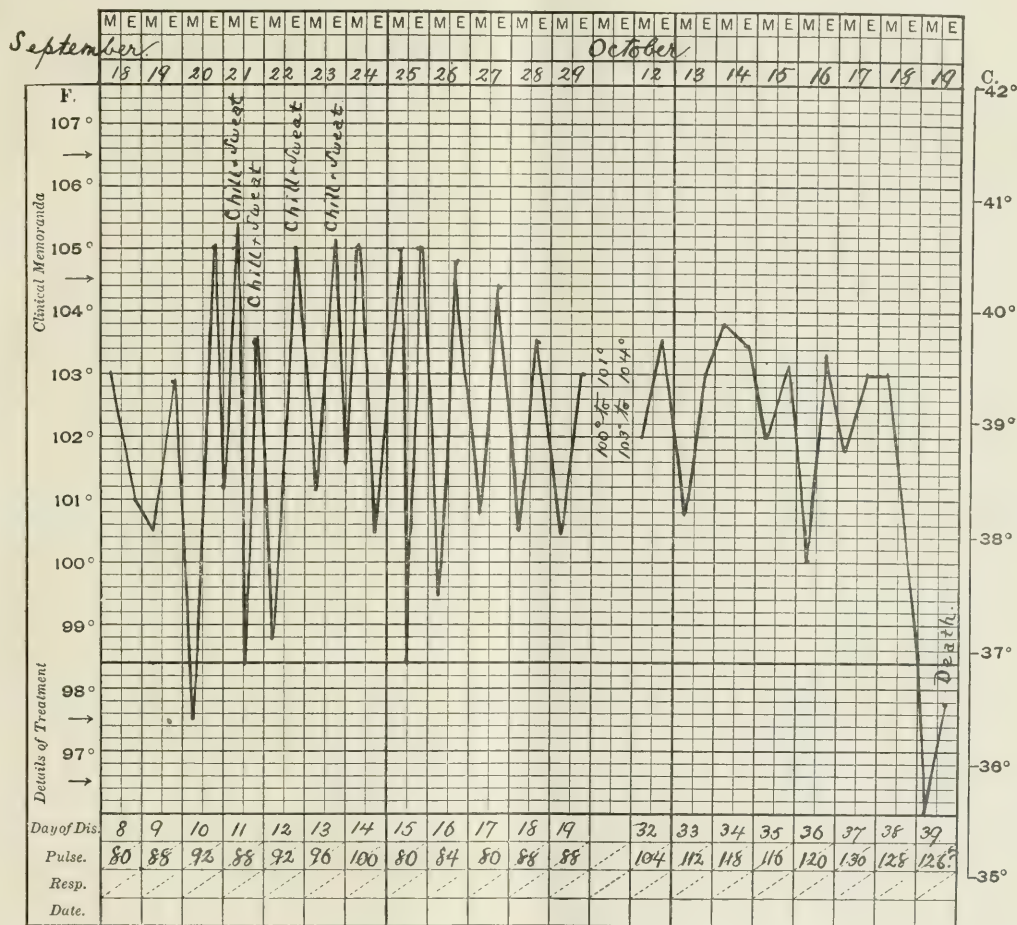
*Family History.*—Unimportant.

<sup>1</sup> Presented before the Johns Hopkins Hospital Medical Society, November 4, 1901.

*Past History.*—Always in good health. No rheumatism or infectious diseases. Habits regular, hard worker, usual weight 160 pounds. One year ago had a purulent urethritis without complications which disappeared without treatment. On August 8, 1901, he came to the Genito-urinary Clinic

with a purulent urethritis of five weeks' duration. The note on that date upon his history card reads, "Purulent discharge from the urethra, intra- and extracellular diplococci, typical gonococci. Three small, healing sores at the frenum of the glans penis, inguinal glands enlarged and tender."

after the second gonorrhoeal infection, with a severe chill, headache, giddiness, and general prostration. For a week the chills continued, occurring sometimes twice a day, and on September 18 he returned to the Genito-urinary Clinic. He was immediately sent to the medical wards.



There were no other manifestations of disease and the patient was dismissed with the usual instructions. He did not apparently carry out the treatment prescribed, but placed himself under the care of a suburban physician. The purulent discharge continued for about 4 weeks and then "turned to blood." There was no pain on micturition but the penis remained "sore." On account of increasing weakness and malaise he did not go back to work.

*Present Illness.*—Began about September 10, 10 weeks

#### PHYSICAL EXAMINATION.

Tall, fairly well nourished, muscular negro. Weight 136 pounds. Mucous membranes slightly pale; tongue coated.

*Lungs.*—Percussion note clear; breath sounds feeble but everywhere clear.

*Heart.*—Impulse not visible; palpable in the 6th inter-space 7.5 cm. to the left of the mid-sternal line. Dulness to this point; no dulness to the right of the sternum. Sounds everywhere feeble. First sound at the apex has a

distinct murmurish quality. At the base both second sounds short and sharp. Pulse small, weak, irregular and easily compressed; 80 to the minute.

*Abdomen.*—Natural; edge of liver and spleen not palpable. No tenderness in the splenic region.

*Genitalia.*—No sore or scar on the penis. Penis not tender and no discharge from the meatus. Testicles and epididymis normal. Prostate soft and symmetrical; not enlarged or tender. A smear from the urethra shows mucous shreds, a few polymorphonuclear leucocytes, but no gonococci.

*Urine.*—Amber colored, clear, trace of albumin, many hyaline, granular, red-blood-cell and epithelial-cell casts.

*Blood.*—Hæmoglobin, 50 per cent. R. b. c.'s, 3,820,000. W. b. c.'s, 32,850. No malarial parasites. Widal reaction negative.

The character of the fever is best shown by the accompanying chart. The chills, two of which occurred on the same day, preceded the rises in temperature and the sweats were profuse. Early in the disease a slight swelling with

four Erlenmeyer flasks, each containing 150 cc. of bouillon to which 20-30 cc. of hydrocele fluid had been added. On October 4 and 12, 12 cc. of blood were again withdrawn, mixed with 25 cc. of melted agar and immediately plated. In each instance the media remained sterile. On October 18, just 24 hours before death, the median basilic vein was exposed under cocaine and 12.5 cc. of blood removed. This quantity was as nearly as possible equally divided among three tubes, each containing 10 cc. of melted agar, which after gentle mixing were quickly plated, and two slant hydrocele-agar tubes in which there was an excess of hydrocele fluid. A second 12.5 cc. of blood was divided among three 150 cc. flasks of bouillon and one 150 cc. flask of litmus milk. Both aerobic and anaerobic methods of cultivation were employed, with the following results:

Then, cultivated aerobically for 48 hours, colonies identical in appearance and in numbers with those of the original aerobic cultures developed in Plate C and in Tube B.

Aerobic Cultures.	24 Hours.	48 Hours.	72 Hours.
Agar Plate A. 10 cc. agar, 2-3 cc. blood.	Numerous, minute, blue-white surface colonies; as many pin-point deep colonies.	Surface colonies $\frac{1}{2}$ mm. in diameter. Pale blue-grey. About 200 in number.	No change.
Agar Plate B. 10 cc. agar, 4-5 cc. blood.	No visible growth.	Like Plate A. Surface colonies 1 mm. in diameter. 3-400 in number.	No change.
Hydrocele-agar Tube A. 3-4 cc. blood.	No visible growth.	2 minute colonies at the edge of hydrocele fluid and submerged blood clot.	20 white, glistening, circular colonies, some 2 mm. in diameter, at edge of fluid and on surface of agar.
Bouillon Flasks A & B. 150 cc. bouillon, 4 cc. blood.	No growth.	No growth.	No growth

tenderness appeared for a day on the anterior aspect of the right ankle. There was never any tenderness in the splenic region nor was a friction rub ever heard. On September 22, the 12th day of illness, the first cardiac sound was replaced at the apex by a loud systolic murmur which rapidly increased in intensity and which could finally be heard over the body of the heart and out in the axilla. Visible pulsation appeared in the second and third left interspaces and the shock of the second pulmonic sound could easily be felt. Gradually the patient began to loose ground, the heart action became more irregular, the pulse more rapid, and the respirations hurried. The red-blood-cell count fell to 2,368,000, the hæmoglobin estimation to 30 per cent. On October 17 an area of pulmonary consolidation was made out in the left axilla, the sputum became blood tinged and the leucocytes, which had ranged between 20,000 and 30,000, rose to 47,000. On the 18th the patient became comatose and died 24 hours later.

#### BACTERIOLOGY.

*Blood Cultures.*—Cultures were made from the blood on five separate days. On September 24 and 27, 12 cc. of blood were withdrawn from a vein in the elbow and divided among

Anaerobic Cultures.	72 Hours.
Agar Plate C. 10 cc. agar, 3-4 cc. blood.	1 pin-point surface colony.
Hydrocele-agar Tube B. 3-4 cc. blood.	No growth.
Bouillon Flask C. 150 cc. bouil., 4 cc. blood.	No growth.
Litmus Milk Flask. 150 cc. milk, 4 cc. blood.	No growth.

Coverslip preparations of colonies taken at random from all the media showed in every instance a diplococcus, never definitely biscuit-shaped, often lance-shaped, and frequently irregular in size and form. With the ordinary aniline dyes the organisms stained unevenly, some appearing as mere shadows, others being brilliantly colored. Young and old colonies alike were decolorized by the Gram method of staining. A marked viscosity was characteristic of all the colonies, the smaller ones adhered bodily to the needle point, the larger ones were drawn out into threads 3 to 4 mm. in length. When detached from the hydrocele agar they floated intact upon the surface of the hydrocele fluid.

The organisms failed to grow when transferred to hydrocele-agar (owing, possibly, to early death of the original colonies), but of 14 plain agar tubes inoculated, a few minute colonies developed upon two. On a mixture of human blood and agar they grew luxuriantly, some of the colonies reaching 2 mm. in diameter, and all exhibiting the same pale blue-grey color of the original blood-agar cultures. Inoculation upon potato, gelatine, glucose-agar, Loeffler's blood-serum, and into bouillon and milk proved negative. The organism could not be cultivated beyond the second generation and the original cultures lived but for a few days. No inoculation experiments were made.

#### PATHOLOGICAL REPORT.

*Autopsy 1810.*—J. A., aged 20, colored; from the service of Dr. Osler.

Autopsy performed by Dr. MacCallum 19 hours after death, on October 20.

*Anatomical Diagnosis.*—Vegetative endocarditis affecting the mitral valve. Œdema and induration of the lungs. Acute splenic tumor with infarction. Subacute nephritis with infarctions.

*Pericardial Cavity.*—The serous surfaces are smooth and glistening. It contains a little clear fluid.

*Heart.*—At the apex of the left ventricle is a muscle-like tendinous patch, and similar smaller ones are present over the right ventricle. The cavities of the right side of the heart are filled with chicken-fat clot chiefly. The valves are normal. The left auricle contains dark clot and its appendix is empty. Projecting into the left auricle is a mass of opaque yellowish-pink material. Upon opening the left ventricle there are found to be huge vegetations on the mitral valve, and on the posterior segment is an especially large one elevated 3 cm. above the valve and is 4 cm. in width. The anterior valvular segment is hollowed out towards its ventricular cavity, crater-like, and filled with a vegetation of a yellowish color, its extremities being friable and almost translucent in appearance; it measures 2 cm. in diameter and 6 mm. in height. Elsewhere the mitral valve is fairly delicate and its endocardium smooth. The myocardium is pale and flecked with yellow opaque areas. The muscle is firm.

*Spleen.*—Weighs 200 grams. Color, magenta-red. Consistence soft. Malpighian bodies are readily visible; likewise the trabeculae and vessels. Its upper end shows a large flabby mass covered by a thin layer of fibrin, of an opaque yellow color and surrounded by a zone in which small hemorrhages are seen. On section it is necrotic and bounded by a deep red zone, and extends into the splenic substance.

*Kidneys.*—Show evidences of subacute nephritis, and contain several anæmic infarcts.

Prostate, urethra, testicles, intestines and other tissues and organs, apparently normal.

*Microscopic Appearances: Heart.*—The epicardial tendinous

patch consists of a loose mass of soft connective tissue covered by a sort of cubical endothelium, which in some places is even heaped up in several layers. In the depths of the patch are curious tubular structures lined by similar cells, possibly merely crypt-like downgrowths of the covering cells.

*Heart Muscle.*—This shows some œdema, but otherwise no especial abnormality. In one place, however, its vessels contain very many leucocytes.

*Kidney.*—There is extensive fatty and parenchymatous degeneration of the tubular epithelium. That of the glomerular capsules is often swollen and desquamated. There are frequently leucocytes in the capsules, and the tubules often contain great numbers of such polynuclear cells in addition to the coagulated fluid and hyaline casts which occur in some. Some tubules contain considerable numbers of red corpuscles. There are no proliferative changes in the kidney but there are foci of lymphoid cells in the portion near the papillae.

*Lung.*—There is coagulated fluid and some desquamated epithelium in the alveoli. The capillaries are distended and tortuous. In some alveoli there are plugs of fibrin which are overgrown by the epithelium and are undergoing organization. These seem to occur singly and perhaps represent the organization of exudate in single alveoli.

*Spleen.*—The Malpighian bodies are not enlarged. There is no increase in the number of parenchymal cells. The infarcted area shows complete necrosis of the tissue, the architecture of which, however, remains. The area is sharply marked out by a zone of fibrin, but there is no marked inflammatory reaction.

*Liver.*—Shows no abnormality beyond excessive amount of fat in the epithelium. The blood in the capillaries shows the existence of a leucocytosis.

*Urethral mucosa* shows no inflammatory reaction.

*Urinary bladder* likewise shows no sign of inflammation.

*Prostate gland and epididymis* are seemingly normal.

#### BACTERIOLOGICAL RESULTS POST-MORTEM.

At the autopsy, plate cultures were made with hydrocele-fluid agar from the heart's blood, the vegetations on the mitral valve, the splenic infarct, the urinary bladder, the urethra and the seminal fluid in the vesiculæ seminales. Coverslip preparations were made also from the above situations, excepting that of the heart's blood.

The plates were incubated for 48 hours in the thermostat at 36.5° C., and complete studies made of the various organisms developing thereon, from which the following results were obtained:

*Mic. gonorrhææ* from the heart's blood and the vegetations on the mitral valve.

*Streptococcus pyogenes* from the kidney, urinary bladder, and urethra.

*Bacillus coli* from the heart's blood, kidney and urinary bladder.

Cultures made from the splenic infarct and the spermat-

fluid remained sterile, as did an uninoculated hydrocele-fluid agar plate, showing the hydrocele fluid to be germ-free.

Coverslip preparations made from the vegetations on the mitral valve show some fibrin, red-blood corpuscles, leucocytes, and numerous micrococci. These latter are for the most part found lying outside of the polynuclear leucocytes, and are grouped in pairs and clusters most frequently, less often singly or in tetrads. Considerable variation in size exists, some cocci being tolerably large, whilst others are rather small. The typical coffee-bean shape is only met with in the intracellular forms. The number of cocci lying within polynuclear leucocytes varies greatly, some cells being crammed full, whilst others contain from four to eight cocci. The cocci are decolorized when stained by Gram's method.

Upon none of the other coverslip preparations were microorganisms resembling definite cocci to be found.

The proof that the organism isolated from the blood and vegetations was the gonococcus, rested upon the following facts: The organism grew upon hydrocele-fluid agar and in hydrocele-fluid bouillon, or upon media to which was added human blood. It failed to grow upon any of the usual laboratory media. It decolorized by Gram's method of staining, both in cultures and from the vegetative growth. In addition, inoculation of a guinea-pig intraperitoneally with 1 cc. of a 48-hour old hydrocele-fluid bouillon culture resulted in the death of the animal within eight days, and, as Wertheim<sup>2</sup> found in some of his experiments, there existed only the smallest evidences of a peritonitis, and cultures and coverslips were both negative.

In reporting his case of gonorrhœal arthritis with isolation of the gonococcus from the blood (see table), Unger suggested that in order to cultivate the gonococcus in this way it is necessary, as in isolating the typhoid bacillus and the pneumococcus, to use a large amount of blood and to dilute the blood with a still greater quantity of medium. A glance at the accompanying table compiled from all the undoubted cases of gonorrhœal infection which we have been able to collect, brings out the following points regarding methods of blood-culture employed:

1. In almost every instance a small amount of blood was used.
2. A very slight dilution of the blood, or no dilution at all was made.
3. Dilution with even a small quantity of plain bouillon, probably by thinning the serum, prevented the growth of the gonococcus.
4. In the fatal cases, as well as in those which recovered, practically the same method of culture was employed.
5. In the fatal cases the method of slight, or non-dilution, gave positive results as early as the 9th, and possibly the 11th, day before death.
6. In our case the agar plate representing the least dilution, and the largest amount of blood, gave the greatest number of colonies, about 100 for each cc. of blood.

As regards the large quantity of blood deemed necessary for success in blood-culture work in typhoid fever and lobar pneumonia, Unger's observations thereon are correct. On the other hand, Prochaska<sup>3</sup> has lately reported four cases of pneumococcus septicæmia, without pulmonary consolidation in three, wherein he cultivated the specific organism from such small quantities of blood as 0.5 to 1 cc. And in connection with cultures in such diseases, the rule has been to liberally dilute the given quantity of blood with broth, etc., the idea being that by this means the bactericidal influence of the blood would be counteracted, thus rendering more certain the growth of any organisms present in few numbers, or any in an enfeebled state. Whether this idea is a correct one is open to question, for it has been demonstrated by Gwyn,<sup>4</sup> and Brion and Kayser<sup>5</sup> that the so-called paracolon bacillus can be grown by smearing the surfaces of agar tubes with a few cubic centimetres of freshly drawn blood; and Dr. Longcope of the Pennsylvania Hospital in Philadelphia informs us that he always is successful in cultivating the pneumococcus from the heart's blood of pneumonia cases at autopsy, by simply mixing 4 cc. of the blood with 10 cc. of melted agar and plating the same. That this idea of liberal dilution may be erroneous will also be noted presently in connection with the culture of the gonococcus.

In contrast to the accepted technique employed in making blood-cultures in typhoid fever and pneumonia we wish to emphasize some facts brought out in the analysis of the cases presented in Tables I and II. Firstly, all successful cultures were attained where the blood was diluted in low degree, but in our case where the dilution was great, no growth occurred. Of course, in the first four of our attempts it is quite possible that no organisms were present in the blood at those periods, yet in our last attempt it will be seen that failure attended high dilution, but was very successful in low dilution. Secondly, in cases 1, 2 and 3 cited in Table II, and case 3 in Table I, it will be seen that no dilution whatever seemed necessary to bring about a positive result, as the blood was simply spread over solidified agar.

It now becomes apparent that for the successful culture of the gonococcus several factors must be taken into consideration. In the first place, on account of the very parasitic nature of the organism, the albuminous food (i. e. the blood) must be present in abundance, a high degree of dilution apparently robs the bacteria of the necessary amount and no growth results. Secondly, it would seem preferable that solid media be employed instead of fluid in effecting the isolation, because in case 4, Table I, and from other laboratory observations of our own upon this point, it appears that this organism thrives better, other things being equal, under conditions of freest access to oxygen, and this requirement is much better met in the thin layer of medium in the Petri dish than in the tube of bouillon where the blood soon clots and sinks to the bottom of the tube. Thirdly, the time in

<sup>2</sup> Deutsch. med. Woch., 1902, May 22, p. 372.

<sup>3</sup> Johns Hopkins Hosp. Bull., 1898, vol. IX, p. 54.

<sup>4</sup> Münch. med. Woch., 1902, April 15, p. 611.

<sup>5</sup> Wertheim (E.), Verhandlungen der deutsch. Gesellsch. f. Gynäk., IV. Kongress, 1891, p. 346.

the course of the disease during which one might expect to obtain positive results. This is indeed a doubtful factor, but recognizing as we do the scarcity of available data by which to form any definite opinion upon the subject, it seems suggestive in the light of the data in our list of cases that in the endocardial infections, which were progressively going on to a fatal termination, the gonococci appeared in blood drawn, upon the average, five days before death, but in one case as early as the eleventh day, and in another, our own, as late as one day before the exodus, dependent seemingly upon the time of disintegration of the usual large friable vegetative growth by the blood stream. But in those infections classed in Table II the authors were successful in isolating the gonococcus during the height of the inflammatory processes.

## CONCLUSIONS.

1. To cultivate the gonococcus from the blood during life, it is neither necessary to use a large amount of blood, nor to greatly dilute the blood, nor to employ any specially prepared medium.
2. It is more advantageous to mix the blood with melted agar and plate the same, than to use fluid media where oxygen supply is more restricted.
3. That the time selected for making the culture, taken in relationship to the course of the disease, may be a factor of sufficient importance to be taken into consideration.
4. Compared with its action upon the typhoid bacillus and pneumococcus, the bactericidal power of the blood seemingly has little effect in retarding growth of the gonococcus.

TABLE I. BLOOD CULTURE IN GONORRHOEAL ENDOCARDITIS.

	Sex.	Age.	Illness.	Heart lesion.	Other lesions.	Day before death of blood culture.	Amount of blood used.	Method of Culture.	No. of Colonies.	Result of Illness.
1. Thayer & Blumer. Johns Hopkins Hospital Bulletin, 1896, vii, page 57	Female.	34	18 wks.	Mitral valves.	Arthritis, nephritis, hæmorrhagic infarcts of spleen and lungs.	9 & 4	5 cc. (?)	1/3 blood, 2/3 melted agar plated.	Very numerous	Death.
2. Thayer & Lazear. Journal of Experimental Medicine 1899, vol. iv, p. 61	Male.	19	7 mos.	Tricuspid valves.	Arthritis, nephritis pericarditis.	3 1 6	2 cc. 2 cc. 3 cc.	Mixed with 4 cc. melted agar. " " " " " " " "	Very numerous.	Death.
3. Byelogowoy. Bohnitché Gazette, 1899, No. 4, p. 137.	Male.	32	2 mos.	Tricuspid and aortic valves.	Pyelitis, hæmorrhagic infarcts of spleen and kidneys.	11(?)	1 cc.	Spread on 3 plates of glycerine-hydrocele-agar.	20	Death.
4. R. J. Wilson, N. Y. University	Female.	38	5 wks.	Aortic valves.	Arthritis, salpingitis, endometritis.	8	3 cc.	1-1½ cc. blood, 6 cc. melted agar plated.	8	Death.
Bulletin of Medical Sciences, July 1901.	Male.	29	7 wks.	Mitral and aortic valves.	Nephritis, infarction of lung and spleen.	7	5.5 cc. 2½ cc. 2½ cc.	1-2½ cc. blood, 6 cc. bouillon. 1½ cc. blood, 6 cc. melted agar and glucose-agar plated. 1½ cc. blood, 6 cc. bouillon.	No growth. 9 No growth.	Death.
5. Harris & Johnson.	Male.	20	11 wks.	Mitral valves.	Transient arthritis, nephritis, infarctions of spleen and kidney.	26 23 15 7 1	12 cc. 12 cc. 12 cc. 12 cc. 12.5 cc.	3 cc. blood, 150 cc. hydrocele bouillon. 3 cc. blood, 150 cc. hydrocele bouillon. 25 cc. melted agar plated. 25 cc. melted agar plated. 3-4 cc. blood, 150 cc. bouillon. 3-4 cc. blood, 150 cc. milk. 2-5 cc. blood, 10 cc. melted agar.	No growth. " " " " (3 plates) 2-400 in each plate, (2 tubes) 20 in each tube.	Death.
								3-4 cc. blood, hydrocele-agar slant.		

TABLE II. BLOOD CULTURE IN OTHER GONORRHOEAL INFECTIONS.

	Sex.	Age.	Lesions.	Amount blood used	Method of Culture.	No. of colonies.	Result.
1. Ahmann. Archiv. für Dermat. und Syphilis, 1896, Bd. xxxix, p. 323.	Male.	32	Polyarthrititis, myositis, teno-vaginitis.	1 cc.	Spread on 4 ascitic-agar plates.	30.	Not stated.
2. Colombini. Centralbl't für Bakteriologie, 1898, Abt. I, page 955.	Male.	28	Epididymitis (abcess), inguinal bubo, parotitis.	1 cc.	Spread on plates of ascitic and urine-agar.	Not stated.	Not stated.
3. Panichi. La Settimana Medica, August, 1899. No. 34.	Male.	31	Polyarthrititis.	2 cc.	Spread on glycerine-agar plates.	Numerous.	Recovery.
	Male.	32	Polyarthrititis.	2 cc.	Spread on glycerine-agar plates.	Numerous.	Recovery.
4. Unger. Deutsch. med. Wochenschrift, 1901, No. 51. p. 894.	Male.	18	Polyarthrititis.	10 cc.	5 cc. blood, 20 cc. ascitic fluid bouillon, 1:2.	Not stated.	Recovery.

## A CASE OF TABETIC VERTEBRAL OSTEO-ARTHROPATHY, WITH RADIOGRAPH.

BY W. B. CORNELL.

The patient, H. G., general medical number C 22,762, presented himself June 2, 1902, in the neurological clinic of Dr. H. M. Thomas, who has kindly asked me to report the case. An examination was first made in the dispensary and afterward finished in the wards of Johns Hopkins Hospital. A summary of the dispensary and hospital histories is here given.

H. G., æt. 55. Male; white; a native of Virginia; peddler. Complaint, locomotor ataxia. Family and personal history is unimportant except for an initial syphilitic lesion when the patient was 22 years old, for which he received treatment from a druggist. No secondary symptoms are remembered. The first symptoms of tabes came on at 47. After a severe attack of diarrhoea he felt a sensation of constriction about the thighs, and shortly afterward around the waist. Shooting pains soon followed which were worse on exposure to the weather. During the first year of his disease he had difficulty in starting the flow of urine; this was followed by incontinence of urine, and occasional incontinence of feces. While the ataxia was developing there was a period of marked increase of venereal appetite which was gradually supplanted by a loss of sexual power, desire being retained but the power of erection being lost. Occasionally there was incontinence of semen. In two years his ataxia had reached the extreme grade shown by present state. Five years ago his attention was first called to a lump in his back. There had been no trauma and the lump seemed to have appeared suddenly. Since then its size has slowly and gradually increased. There has never been any pain in this mass. His hips have at times become painlessly dislocated, especially on going up stairs. Blisters have developed under the toenails, causing the nail to break off half way to the base. His finger nails are also brittle. His left great toe was amputated for a slight wound which refused to heal. The lightning pains still persist. He walks with difficulty on crutches.

On examination the patient is bright and intelligent. He is of small stature and poorly nourished and has lost weight. His pupils are unequal, left is slightly dilated, while the right is contracted (spinal myosis). Both react slowly to light, but actively to accommodation. Vision is good in the left eye, fair in the right. There is extreme incoordination of legs and a definite ataxia also in the arms. Jerky, choreiform movements occur in the muscles of head, arms and hands.

Masseteric reflex is present; triceps reflex also present but diminished. No pain on pressure over the ulnar nerve at elbow (Biernacki's sign). Wrist, epigastric, cremasteric, patellar, and plantar reflexes are entirely absent.

There were most marked alterations in cutaneous sensation. The head, neck, and areas running down the shoulders

and outer side of the arms to elbow were the least affected. The rest of the arms, body and legs showed either entire anæsthesia to pain, temperature and touch or some paræsthesia. Anæsthesia to touch was most widespread; to cold almost as much. Pain and heat in general occupied the same areas, but heat sensation was not so much involved as pain. The soles and dorsum of the feet showed delayed transmission of pain, fully five seconds being required before the point of a pin was perceived to be sharp. It was not felt first to the touch. Various paræsthesiæ were noted. A prick on one knee would be referred to the other knee. On drawing a pin-point over the back, a sensation of cold was produced. A pin prick on the foot felt like something burning to the patient. A very hot test tube was felt as "sharp" over the legs and body; not until the neck region was reached did the patient say "hot." A sensation of touch was felt occasionally for some seconds after the object had been withdrawn. Muscle sense in arms was markedly affected; in legs entirely absent. There was complete astereognosis in the hands.

There are numerous scars on elbows, arms, body and soles of feet. The latter probably representing healed small ulcers, the former ulcers of traumatic origin.

In the right lumbar region of the back is a large tumor mass, which appears to be connected with a scoliosis to the right and a kyphosis of the spine at this point. On palpation of this lump with the patient lying on his stomach a superficial fluctuation is perceived which also extends upward as a band 5 cm. wide on the right of the spinal column to a point midway of the scapula. On deep palpation bony hardness is felt and some small, loose bodies which slip under the fingers. Deep crepitus and abnormal motility at the lumbo-sacral joint are obtained on rotating the spine on the sacrum. There is a compensatory dorsal scoliosis to the left; the pelvis is tilted upward in front and rotated forward on the right. The right iliac crest is distinctly higher than the left. The abdominal walls are loose and flabby. There is a marked increase of lateral motion of the body to the left; to the right motion is restricted apparently by the bodies of the lumbar vertebræ impinging on the iliac crest. No other joints show any trophic alteration.

Dr. W. S. Baer, who has loaned the skiagraph plate, has also been kind enough to append a description of the condition as elucidated by the X-ray.

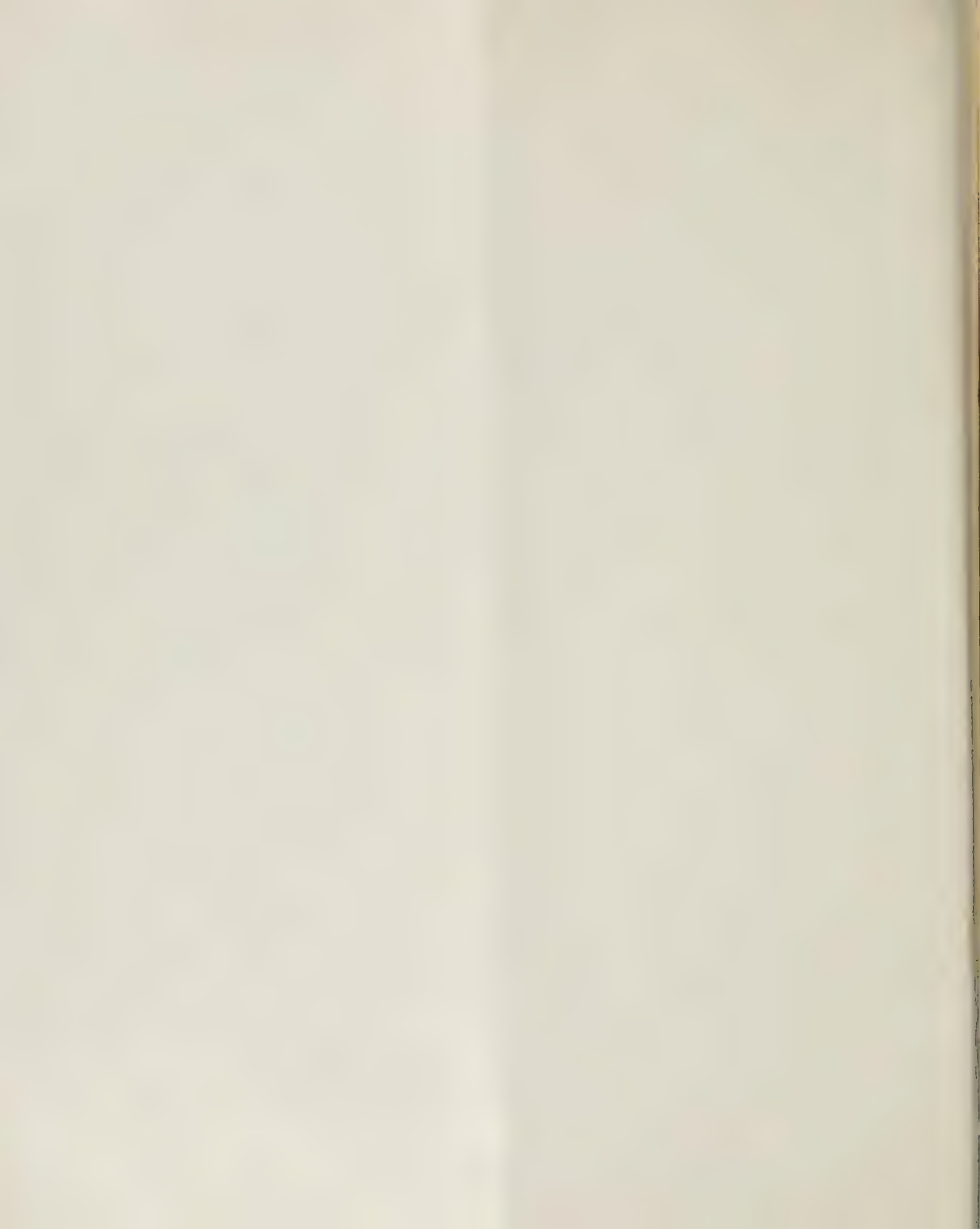
"The pathological picture presented by the radiograph shows a marked scoliosis of the spine with a rotatory lateral curvature. The vertebræ affected include those between the XI dorsal and the sacrum. There seems to be a destruction of bony tissue along the left side of each vertebra from the XII dorsal to the IV lumbar. The intervertebral cartilages seem to have been destroyed, especially between



Photograph showing the osteo-arthropathy.



Radiograph showing the affected vertebrae.



the last vertebra and the sacrum where the sacro-vertebral space is four times its normal size. Along the transverse processes of the left side from the I lumbar to and including the sacro-iliac articulation, are large masses of exostoses. The radiograph also shows the outline of an abscess cavity running up on the right side along the spinal column from the lower margin of the III dorsal. There is another abscess to the left of the lumbar vertebra outside of the sacro-iliac joint; the pelvis seems normal."

The condition thus described will be seen quite analogous to that shown by other joints of the body in association with tabes. The rarity of tabetic spinal osteo-arthropathies will be appreciated on running through the literature on the subject. Charcot, in his original descriptions, mentioned not a case. Rotter,<sup>1</sup> in his classical monograph, describes 112 tabetic joints, none occurring in the spine. The same is true of Flatow's 149 Charcot's joints, and Weizsacker's 100. Kredel in a series of 132 cases of tabes, Bramwell in 155, Riley in 61, Bonar in 286, and Matschutkowski in 1662, do not mention any arthropathy of the spine. Kroenig,<sup>2</sup> however, called particular attention to this condition in 1888 when he reported three cases, one of which was first published in 1884. After this, other cases were published and in 1900 Jean Abadie,<sup>3</sup> after a careful search, was able to collect 14 cases from the literature and from material at hand. None of these cases occurred in America, nor have I been able to find any since reported from American clinics. Three of the cases collected by Abadie (two being those of Pitres and Vaillard,<sup>4</sup> and the third his own) were complete with clinical and post-mortem observations. A fourth consisted only of a museum specimen of six vertebrae from a tabetic, and unaccompanied by clinical details. The remaining 10 presented clinical observations more or less complete, one of which is only a drawing of the back of a tabetic woman.

The following is an analysis of the cases collected by Abadie, and our present one, making 15 in all:

*Syphilis* was present in 5 (38 per cent), absent in 6, probable in 2.

<sup>1</sup>J. Rotter: Die Arthropathien bei Tabikern, Archiv. f. klin. Chirurgie, 1887, Bd. 36.

<sup>2</sup>G. Kroenig: Wirbelerkrankungen bei Tabikern, Zeit. f. klin. Med., 1888, p. 51 ff.

<sup>3</sup>J. Abadie: Nouv. Iconograph. de la Salpêtrière, T. XIII, 1900.

<sup>4</sup>Pitres et Vaillard: Bull. de la Soc. de Biologie de Paris, Nov. 1885, (cit Abadie).

*Sex.*—10 were males, 4 females. Comparing this with the much greater frequency of tabes in the male (91 per cent Bramwell<sup>5</sup>) it would seem from these cases that vertebral arthropathies are more common in women.

*Age.*—At observation 10 (78 per cent) were between 50-60, 35 the youngest, 66 the oldest. Age of onset of tabes in 9 (70 per cent) was between 35-45; 23 and 45 were the extremes. Age at onset of spinal arthropathy in 11 (84 per cent) was between 45-55, of these 8 (61 per cent) were between 50-55. Seven years was the earliest, 22 the latest, for the spinal arthropathy to develop after the onset of tabes. In no case did it develop at the onset even if another arthropathy was the initial tabetic symptom. Thus the conclusion is justified that the vertebral column resists attack the longest, and if affected at all it is commonly so at 50, or 12 years after the onset of tabes.

*Ataxia* in 7 was of extreme grade; in 5 moderate; in 1 very slight.

Other arthropathies occurred in 8 (61 per cent); in 5 the spine alone was affected.

*Trauma* was the apparent immediate cause of fracture of the vertebrae or other deformity in 5 (38 per cent). In 7 there was no exciting cause. In one case there was a spontaneous fracture, the patient feeling a crackling sensation in the spinal column and thereafter first noticed his deformity.

*Curvature.*—Scoliosis was the most frequent. Of this the dorso-lumbar variety occurred 7 times, cervico-dorsal 4, dorsal 3, lumbo-sacral 1, multiple scolioses 1. *Kyphosis* was the next in frequency; in the dorsal region 3, in dorso-lumbar 2, in cervico-dorsal 2. *Lordosis* occurred in dorso-lumbar region 2, inferior dorsal 1. A knuckle was present in 5 cases; most frequently the V lumbar was involved. The *pathology* seems quite analogous to that which has been described in relation to tabetic arthropathies in general. The hypertrophic variety, with the formation of osteophytes, exostoses, and occasionally ankyloses is most frequent. This is the picture in the main given by the radiograph in our case, with the addition of a periarthropathic involvement of the soft parts.

Finally, I desire to thank Dr. Thomas for kind help and the opportunity of publishing this case; and also Dr. Baer and Mr. Bassett for the photographic plates.

<sup>5</sup>Byrom Bramwell: Brain, Spring, 1902.

## THE JOHNS HOPKINS HOSPITAL BULLETIN.

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- CHARLES RUSSELL BARDEEN, M. D. A Statistical Study of the Abdominal and Border-Nerves in Man.—*The American Journal of Anatomy*, February, 1902.
- LEWELLYS F. BARKER, M. D. Medicine and the Universities.—*American Medicine*, July 26, 1902.
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## PROCEEDINGS OF SOCIETIES.

### THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Monday, March 3, 1902.

The meeting was called to order by the President, Dr. Osler.

#### Exhibition of Medical Cases. DR. McCRAE.

This case is one of an interesting type of anaemia. The patient is a farmer aged 39 years, who complains of shortness of breath and stomach trouble. His previous and fam-

ily history is negative. The present illness dates back about one year when he had what he thinks was an attack of typhoid fever. After that he was troubled with nausea and vomiting on arising in the morning and had to give up his work. He noticed some time ago that he stumbled in walking, but he attributed this to his weakness.

On examination he shows some pallor but is well nourished. He is exceedingly weak and short of breath on any exertion, fainting if it is carried very far. In the mouth

there is slight pyorrhoea. The thorax and abdomen are negative. The specific gravity of the urine is low and there is a considerable quantity of albumen with a number of casts. The hemoglobin is 27 per cent, red cells 1,400,000, a color index of about one, and leucocytes about 7000. The differential count shows a percentage of polynuclears of 88 per cent, small mononuclears 8 per cent, large mononuclears 2 per cent, and 2 per cent of eosinophiles. The red cells show very little change, perhaps some deformity, and only one nucleated red cell, a normoblast, was found.

The condition suggests a primary anaemia, but the fact that he has such a large amount of albumen in the urine suggests the possibility of an anaemia due to chronic nephritis. The result of an examination of our cases of pernicious anaemia has shown not a case with more than a mere trace of albumen in the urine. This suggests that if this case be a primary anaemia there must be something in addition. It seems most likely that there is a chronic nephritis with an anaemia of so-called primary nature and not secondary to renal disease. The coincidence of these two conditions has not been common in our cases.

#### **Exhibition of Surgical Cases. DR. TINKER.**

##### **(a) Compound Outward Dislocation of Elbow, with Excision.**

The first case about which I wish to speak I shall be unable to show to-night, because he is now an inmate of an insane asylum. I saw the patient last summer after a severe injury of his elbow, which was very much swollen. The doctor in charge of him thought he had reduced a fracture and put the arm up in a plaster cast for 11 days. On taking it out, however, he found a great deal of deformity and I was called to wire the fracture. The condition of the elbow at this time was as follows: The inner condyle of the humerus was sticking out through the skin on the inside of the arm, the break being about 3 cm. long, the olecranon process projected farther back than normal, the radius could be felt on the outside of the arm and by rotating it the position of the head of the radius could be made out. The triceps tendon was also more prominent than usual. From the signs it was evident that there had been a partial dislocation outwards. The arm had been out of position for 11 days, practically all of the ligaments about the joint had been torn, and so, when I attempted to reduce the dislocation, it was easy to restore the bones to the proper position, but they would not remain there. It was evident therefore that the man would have a joint of very little use to him without operation.

The opening over the inner side of the joint was enlarged, and after a resection had been done the arm was put up in a plaster which the patient kept on for 5 or 6 days and then deciding that he did not like it he rubbed the cast on an iron bedstead and tore the bandages off. He infected the wound but fortunately not so badly as to cause serious trouble.

Partial outward dislocations of the elbow are extremely rare, an unusual form and degree of violence being necessary to produce this injury. It was the first case of outward dislocation of the elbow that I had ever seen, and on looking

up the subject after getting home I found according to Stimson that only 5 cases of this kind had been reported. On going over the literature a little more carefully, however, I find that perhaps a dozen cases have been reported. A series of experiments upon the cadaver by Nicolodoni have shown that by partially flexing the arm, then pronating the forearm and using force on the hand it is possible to cause a dislocation either outwards or inwards. As to the treatment, 6 cases of this kind have been reported by Hueter, who found it necessary in all to do a resection because the ligaments are of necessity torn away.

##### **(b) Fracture of Base of Skull; Haematomyelia; Compound Comminuted Fracture of Lower Jaw, with Wiring and Recovery.**

#### **Asthenic Bulbar Paralysis or Myasthenia Gravis. DR. THOMAS.**

This patient has been in the ward since the 8th of February in Dr. Osler's service. He is 39 years of age and gives an excellent family history with nothing particular in his personal history. He was well up to the first of February of this year, when he noticed difficulty in swallowing; that is, after he had passed the food back to the pharynx he had to make a great effort to swallow it. The next day he felt a stiffness in the neck and on the day following he noticed that the tongue was affected. On the 5th he had difficulty in speaking.

On admission he complained particularly of the difficulty in eating and speaking. The food had a tendency to collect between the cheek and the teeth, and there was difficulty in getting it back into the pharynx on account of the condition of the tongue, and when he got it there it was difficult to swallow it. He complained of very little difficulty with the muscles of the limbs. He had noticed that the right eyelid began to droop. Examination showed him to be apparently a healthy man. There was nothing abnormal in the fundus of the eyes. A slight ptosis is evident and he sometimes sees double upon looking at a distance. In eating or speaking he does well at first and gradually fails. He can sometimes count up to twenty or more before tiring out, but to-night he cannot. His condition varies from day to day, but he is always better in the morning than in the evening.

The muscles most easily tired are the masseters, and to-night he has very little power in these. At any time these muscles soon tire out so that after a few repeated movements you can allow him to bite down upon your finger as hard as he can without danger of being hurt.

He can raise his arm above his head perhaps five or six times but then fails to do so. On electrical stimulation the muscles at first act well, but with the Faradic current the reaction soon becomes less and less marked. He has not had any attacks in which there was difficulty in breathing.

The condition is a very typical example of a very rare disease.

The picture is one of bulbar paralysis, and such patients were formerly so classed. Some of these cases in which the symptoms improved have been reported as recovering from

bulbar paralysis, while other cases which died and in which no anatomical lesions were found, have been recorded as cases of bulbar paralysis without anatomical lesions. It was soon found, however, that this class of cases had peculiar symptoms and the condition came to be known as asthenic bulbar paralysis, myasthenia gravis, and by many other names.

The disease runs a very varied course, and as the patient has days in which he is better he may have years in which he seems perfectly well; but usually, unfortunately, there are relapses.

The passage of a stomach tube to feed such patients has sometimes brought on the difficulty in breathing and death, or too long muscular effort may bring it on, and I am consequently not willing to test him too far.

We have had another case in the neurological dispensary, a young woman of 24, with very good personal and family history, who was seen in 1894 and then lost sight of.

She first had difficulty in reading and then in swallowing, and when seen showed almost the same condition that you have seen in this patient.

I should like to call your attention to two cases of this disease, one reported by Weigert which showed a metastasis in the muscle from a tumor of the thymus gland; the other a case reported by Goldflam in the current *Neurologische Centralb.* (1902, No. 3), which had been watched for over ten years. Two years before death on excising a piece of muscle he found a curious condition, looking like a metastasis, from something he did not know what. He lost sight of the patient until she died at another hospital from lung trouble which proved to be a tumor with metastasis in the muscles.

DR. OSLER.—I should think, if the case warrants, it would be a simple thing to give the muscles complete rest and feed him by artificial fistula through the stomach instead of using the stomach tube.

DR. THOMAS.—Oppenheimer thinks the tube should be avoided as he had a death from the excitation which it produced.

#### **Exhibition of Patient. DR. SPRATT.**

I have been requested to show this case, as Dr. Mitchell, who was to present it before the Society, is out of the city.

This little girl, aged 5, was admitted to the Hospital with the following history:

Family and past history unimportant.

The patient had had frequent micturition for about two weeks. About five days before admission she had complained of great burning during the act. This continued about two days when urinary disturbance became less marked.

About twenty-five hours before admission she began to complain of abdominal pain. This was late in the afternoon. During the night her pain became more severe and somewhat localized about the umbilicus. Next morning she was nauseated and vomited three times. About the same time her bowels moved as a result of cathartics. Her abdomen was very tender and pain continued during the day.

On admission the following points were noted: She was a rather poorly nourished child, very pale, face had a pinched expression. Pulse 125, rather low tension; temperature 102°; leucocytes 25,000.

She was lying on her right side with thighs flexed on abdomen, and extension of the limbs caused moderate pain.

Respiratory movements were very much restricted, especially in lower half of abdomen.

There was no distention and her abdomen was everywhere tympanitic.

On palpation there was general tenderness which was most marked in right lower quadrant and in left flank. Abdominal muscles were rigid. This appeared to be voluntary and not a true muscle spasm.

Patient pointed to her umbilicus as the seat of pain. The child did not appear as ill as the symptoms indicated.

From the vulva there was a thick creamy discharge which came from the vagina. There was no redness about the urethral orifice and no evidence of enlargement of Bartholin's glands.

Cover slips showed intracellular diplococci which decolorized by Gram.

A diagnosis of general gonorrhoeal peritonitis was made and the patient was prepared for operation.

On opening the peritoneal cavity through a median incision, a small quantity of thick yellow fluid was met with. Peritoneum was reddened, its luster was slightly dulled and numerous small subperitoneal hemorrhages were visible.

Appendix was explored and found to be normal. Douglas's fossa contained about 3 cc. of thick yellow pus.

Both Fallopian tubes were swollen, edematous, blood vessels injected and pus was oozing from their fimbriated extremities.

Cultures and cover slips from tubes and cover slips from pus in peritoneal cavity showed gonococci.

Both tubes were excised, the peritoneal cavity was wiped out with moist gauze and the abdominal wound closed without drainage.

She had considerable nausea following the operation which was very much relieved by frequently washing stomach out.

Her wound was dressed on the tenth day and found healed per primam.

The peritoneum was not washed out, simply wiped out.

She is now very comfortable and so far has had no complications.

#### **DISCUSSION.**

DR. OSLER.—How many cases have you had on the gynecological side, Dr. Hunner?

DR. HUNNER.—There have been 10 cases in the Hospital on both sides. I have collected 31 cases in the literature, 17 of which have been operated upon, 13 recovering and 4 dying.

Of the 14 not operated upon 8 recovered and 6 died. A close review of these cases shows the fact that of the 6 that died perhaps none would have been saved by any form

of treatment. Most of them came into the hospital in a moribund condition.

So one is struck by the fact, as we know by the observation here, that there is a difference between gonorrhoeal peritonitis and peritonitis of other forms; that is with regard to the gravity. The patient is usually very ill for a few days, but suddenly this clears up and she recovers. Of course the important thing in these cases is the diagnosis, and we will undoubtedly continue to operate on these cases because we cannot always be sure of the diagnosis. In this case the diagnosis was made of a general peritonitis due to gonorrhoea, although the doctor's account of the case showed almost a typical picture of appendicitis. By those familiar with the gonorrhoeal diseases, however, a diagnosis should be made almost absolutely in every case and of course the question then as to treatment is always to be considered, and I think if one is certain of the diagnosis that these cases should not be operated upon. If the abdomen is opened on the question of diagnosis the treatment should be similar to that given here. I was very much pleased to note that Dr. Mitchell did not attempt to clean the peritoneum, but merely wiped those intestines in view. Nothing could be gained by handling them or by washing out the cavity. The deposit cannot really be wiped off or washed away, and handling the intestines increases the danger of obstruction. If we continue to operate in these cases we must leave the intestines alone as far as possible.

DR. OSLER.—I should think it would be difficult to refrain from asking to have the patient operated upon, judging from the condition of the two cases admitted to my wards.

Those patients, the first ones operated upon here, were seriously ill, there was no question about peritonitis and I think there was no question about the advisability of operating.

#### **Exhibition of Surgical Cases. A Ninth Case of Gasserian Ganglion Extirpation. DR. CUSHING.**

Since the introduction three years ago in Dr. Halsted's service of a method of extirpation of the Ganglion semilunare by what has become known as the infra-arterial method a considerable number of cases of severe trigeminal neuralgia have been operated upon by Drs. Finney, Mitchell and myself. The operative procedure makes use of the advantages of the direct temporal method of approach to the ganglion, thus avoiding the tedious formation of a Wagner flap and the danger of injuring the meningeal artery which are characteristic of the high Hartley-Krause operation. This low operation is one which to-day is employed in most foreign clinics and the method of procedure differs but slightly in the hands of different operators. Some consider it advisable, however, to ligate and divide the meningeal artery even under these circumstances. Thus, Lexer from von Bergmann's clinic has recently reported 15 cases in which he has done the low operation and ligated the artery. His procedure otherwise differs in no great respect from that which we have practiced. In no instance in our series have

we failed to expose and to remove the ganglion in its entirety without injury to the middle meningeal. To ligate this artery or not as it is exposed in the wound becomes a mere detail.

The majority of these cases have been ones which illustrated the most extreme form of trigeminal neuralgia—the neuralgia quinti major of Henry Head—that form of neuralgia which unrelieved usually leads in time to suicide. If the primary object of the physician is to relieve suffering, certainly in cases of this kind pain in its most aggravated form can be abruptly done away with. The abruptness and completeness of the relief in many cases make it seem almost like a resurrection. Did 9 out of 10 of these cases result fatally instead of a possible 1 out of 10, it would still leave a chance which would be eagerly grasped at by the majority of these sufferers. In this particular patient the operation was performed ten days ago and the incision, the line of which can now be scarcely detected, was made in exact correspondence with the curved scar of an operation performed seven years ago when Meckel's ganglion was removed and the N. infraorbitalis evulsed. The relief, as is usual after peripheral operations of this sort, lasted for a period of only two years. For the past five years he has been a constant sufferer and his condition when brought to the Hospital was truly pitiful. The ganglion was removed in toto and he is now and will continue to remain free from pain. There has been no known case of recurrence of neuralgia after a total extirpation of the ganglion. He has gained seven pounds in the ten days since the operation. It is extraordinary how rapidly these people recover their lost weight when they are once again enabled to take nourishment without the act of swallowing occasioning a paroxysm of pain. One of my cases gained thirty pounds in the first seven weeks after the operation. I bring this case before you simply to emphasize the fact that these operations are not only possible but that the relief would justify the risk even though the mortality were much higher than it is. It seems to be the general impression that it is a difficult and most hazardous performance and even if successful that it may be attended by a possible loss of speech and of vision. The slight retraction of the temporal lobe which the low operation necessitates has never been the occasion in our series of cases of producing any symptoms referable to the brain. In the high Hartley-Krause operation in several reported cases a temporary aphasia has followed a left-sided extirpation. There is always some risk of injury to the eye due to the conjunctival anaesthesia subsequent to the operation. With proper care, however, and provided that preliminary operations upon the infraorbital nerve have not left a slight ectropion of the lower lid, this risk which is largely due to the dryness of the cornea is not a great one. This patient's eye has remained perfectly clear and the slight pressure paresis of the sixth nerve which resulted from the operation has already completely passed away. The risk of losing the eye is really very slight and even were it a cer-

tainty I doubt if any of these patients would shrink from the operation on this account.

#### DISCUSSION.

DR. OSLER.—It is really a difficult thing to get physicians to appreciate the extraordinary benefit of this operation. The doctor, under whose care this patient was, consulted me several times about it and it was with some difficulty that I persuaded him to have the operation performed.

#### Demonstration of Making Celloidin Capsules. DR. HARRIS.

(See BULLETIN for May, 1902, page 112.)

*Monday, March 17, 1902.*

The meeting was called to order by Dr. Hurd.

#### Exhibition of Medical Cases. DR. McCRAE.

The patient I wish to show to-night has been both on the obstetrical and the medical side. She came to the obstetrical department in a condition of eclampsia, having had 7 convulsions prior to admission. The uterus was emptied at once, a small amount of chloroform being administered during the time, and after delivery she had several more convulsions. This was on 2d of February. On February 4 Dr. Lynch suspected that the patient had pneumonia, asked me to see her. When I saw her which was 2 days after delivery and probably the first day of her pneumonia I thought she was in a dying condition. The only hopeful feature in the case was that she had passed through so much already and that patients who have such grave conditions often tend to get well. On the second day of the pneumonia she became a little better and from that time on her recovery was uninterrupted.

Those of you who have been working in the medical wards this winter know how many desperate cases we have had that recovered, but none of them approached this in gravity.

A second point that I want to call attention to is the occurrence of pneumonia after some operative procedure even when no anaesthetic has been given. When an anaesthetic has been given we are often in doubt as to what extent the pneumonia is due to it or to the operation. We have had lately 6 cases of post-operative pneumonia, 5 of which had ether and 1 chloroform, but the latter had not more than 1 dram.

They have all shown an atypical course and signs; in this case the fever which on the first day was 104°, dropped the next day to 100°, rose the next to 103° and then rapidly came down. All of the cases showed rather atypical courses.

#### DISCUSSION.

DR. HURD.—Do you think this case was due to the anaesthetic?

DR. McCRAE.—I think the pneumonia was associated with the operation rather than the anaesthetic inasmuch as such a small quantity of chloroform was used.

DR. LYNCH.—Of the 35 cases of pneumonia which we have seen but one other instance occurred in a case of eclampsia and apparently there was in the first case nothing in connection with the operation to cause the pneumonia. This patient when she came in had considerable interference with respiration and was very much choked up.

DR. HURD.—I would ask Dr. Thomas whether there is is any tendency to lobar pneumonia after the convulsive seizures of epilepsy?

DR. THOMAS.—I know of none.

DR. HUNNER.—In view of the use of local anaesthesia nowadays it is interesting to note that a recent report shows a greater percentage of cases of pneumonia following operations under local anaesthesia than occurs after general anaesthesia.

DR. TINKER.—At the German Surgical Society last year a number of surgeons spoke of this point. Mikulicz reported numerous cases of pneumonia occurring after operations, abdominal for the most part, and showed that the frequency of lobar pneumonia after local anaesthesia was as great as after chloroform or ether. This has not been the experience in this Hospital for we have not had any outspoken cases of pneumonia after local anaesthesia and very few cases in which there has been even an irritation of the respiratory organs.

#### Exhibition of Surgical Cases. DR. MITCHELL.

CASE I. *Tuberculosis of Hernial Sac.*—This boy, five years of age, came into the hospital ten days ago with double complete right inguinal herniae, both of which were readily reducible. His general health was good. His temperature was about 99°. He was well nourished and there was nothing to lead one to suspect any complication. The contents of both herniae seemed to be omentum. The ordinary Halsted operation was done first on the left side. On opening the sac it was found to be empty as far as omentum or intestine was concerned, but was filled with cloudy yellowish fluid and the sac wall was oedematous and studded everywhere with innumerable grayish nodules. This condition extended within the internal ring to the parietal peritoneum and was immediately recognized as tuberculous peritonitis involving the hernial sac. A loop of small intestine was pulled down to determine whether the tuberculous process involved the visceral peritoneum and the intestinal serosa was found to be covered with tubercles quite as thickly as the parietal peritoneum. On the right side the same condition was present except that the wall of the sac was very much thickened and its most dependent portion was converted into a tuberculous mass. The peritoneum was rubbed with iodoform powder and the radical hernia operation completed on both sides.

The boy has done well since the operation except for slight temperature which has ranged between 99° and 100°.

This is the third case in our hernia series in which tuberculosis of the sac has been found, and in none was it suspected before operation. The first case was a small colored girl with an umbilical hernia who died of general peritonitis

a week after the operation. The second was a man aged thirty-nine who was operated upon for a large right inguinal hernia of twenty-one years' duration, which had been irreducible for four days. He had no unusual symptoms before operation and was in good health. There was found at operation extensive tuberculosis of the sac and its omental contents, as well as the parietal and visceral peritoneum, the process being most intense in the lower portion of the sac. The Halsted operation for the radical cure of the hernia was done. Following the operation the patient had an afternoon temperature ranging from  $101^{\circ}$  to  $102.5^{\circ}$  which gradually subsided. His wound healed per primam. He left the hospital apparently well and now, four years since the operation, has had no further trouble.

Tuberculosis of a hernial sac is not a very common condition although the literature, especially the Italian, is abundant. Andrews of Chicago has recently reported a number of cases with a review of the literature. The condition is more common in males and in its general features corresponds to general peritoneal tuberculosis and its treatment is naturally the same. The outlook depends upon its origin and extent. The process may be primary in the sac, or the hernial tuberculosis may be only part of a general peritoneal involvement. The latter condition is more common.

**CASE III. Epithelioma of the Lip.**—This man was admitted in October with an extensive epithelioma involving the whole of the lower lip and part of the upper lip and cheek. It was necessary to remove all the lower lip down to the tip of the chin with a portion of the upper lip and left cheek, extending four centimeters from the corner of the mouth, and the glands of the left side of the neck with the right submaxillary and the submental glands. The problem of getting material for a new lip was a difficult one. On the right side where the cheek was undisturbed it was easy to bring over a flap; but on the left it was necessary to go as high as the outer canthus of the eye and to the ear. In this way a flap was turned down to meet the flap from the right cheek. To cover the chin a flap was brought up from the neck. To get mucous membrane on the newly-formed lower lip a flap of mucous membrane from the upper lip was freed and sutured to the surface of the flap of skin forming the lower lip. This was left as a bridge for ten days when it was freed from its attachment to the upper lip. This flap has grown in both directions until now the whole raw surface of the lower lip is covered over with mucous membrane. The man has now a fairly movable lower lip. The deformity is very slight and there is no evidence of return of the epithelioma.

**Exhibition of Casts of Smallpox and Chickenpox.** DR. B. E. DAHLGREN, Philadelphia.

A large collection of casts made during the various stages of these diseases was exhibited.

Monday, April 7, 1902.

The meeting was called to order by the President, Dr. Osler.

**Exhibition of Medical Case. DR. BUNTING.**

The patient is a salesman aged 31 years, who was admitted complaining of rheumatism in the hip and neck. There is no history of rheumatism or gout in his family and his personal history is negative except for one attack of typhoid fever.

His present illness began 9 years ago with pain in the left hip at times quite severe and accompanied by stiffness of the joint. Though these attacks occurred for 5 or 6 years he was not laid up in bed with them. He was exposed a great deal during bad weather, driving about the country, and he attributed his trouble to this. In a later attack he developed stiffness of the left elbow, right shoulder and both knees, and at one time had an inflammation of the iris.

On admission the physical examination in general was negative for the organs.

The spine is practically rigid, the lumbar curve obliterated and there is only slight motion in the cervical vertebrae. The thorax is almost fixed, the movement on deep inspiration being almost entirely abdominal. The left arm cannot be straightened to its full extent, both knees are involved to some degree and the left hip is ankylosed.

**DISCUSSION.**

**DR. OSLER.**—I asked to have this case shown for a special purpose. As some of you know, there has been a great deal of dispute as to the existence of the malady, described as a separate disease, the malady described as spondylitis of central origin confined entirely to the spine and producing complete stiffening with rigidity of the ribs, complete immobility of the thorax, nerve root pains of great intensity and wasting of the muscles.

Now that condition has been described as a separate and distinct disease and it has been claimed that it is a disease of central origin having nothing to do with arthritis deformans. A few years after the first report of this kind Marie reported a spondylitis associated with ankylosis of the shoulder and hip joints and he too described it as a separate malady altogether. Now the cases we have had here would seem to indicate that it is not at all a separate malady but only part and parcel of that common disease arthritis deformans, that it is nothing more than a special form of this, and that just as arthritis deformans may be confined to the hips or the knees for years so this disease may be limited as described. In one case seen here last year a number of the small joints were also affected. Whether or not the nerves are involved and produce pain depends upon the position of the spondylitis; some of the cases begin with the pains and have wasting of the muscles even before the ankylosis appears.

I am very strongly of the opinion that this is not a sepa-

rate disease but simply a variety of arthritis deformans attacking the spine.

#### Hemiplegia in Pernicious Anemia. DR. OSLER.

I would like to speak of a case that is too ill to show but which illustrates a remarkable and unusual condition of pernicious anemia. A young man of 23 was admitted in November, 1900, complaining of jaundice, shifting pains and shortness of breath. He had a doubtful history of lues, typhoid fever at 18 and a moderate alcoholic record. A year before admission he had suffered a slight sunstroke and was in bed for 10 days but recovered completely. In March, 1901, he began to get weak and had recurring attacks of what was supposed to be jaundice.

On admission he appeared well nourished, his face had a yellowish tint with pigmented areas and the diagnosis could be made on simple inspection. There were the usual vascular phenomena of extreme anemia; the red corpuscles 2,000,000, leucocytes 2420 per cm., haemoglobin 30 per cent, no nucleated red cells, and the temperature normal. He went home in December, 1901, and returned in September, 1902, very weak, with an extreme degree of pallor and the same cardiac features present in all extreme anemias.

The blood features were characteristic.

At first he improved but in spite of the usual treatment (complete rest, fresh air, arsenic and good food) he has steadily failed and the blood sank below 100,000 r. b. c. per cm. On March 24 he began to have fever, a not uncommon symptom toward the close. On April 5 he complained of weakness in the right arm and on the following morning he had a complete right sided hemiplegia and it is to that point I wish particularly to direct your attention.

The nervous features of pernicious anemia which are well recognized, as they occur in a considerable percentage of all the cases, may be divided into three groups. First the cases in which there have been no symptoms of any nervous trouble during life but in which well marked spinal cord changes are discovered post mortem; secondly a group in which there are spinal symptoms during life; and thirdly a group in which the spinal cord symptoms initiated the trouble and a pernicious anemia occurs later. We have had no instance of the last group, but a number of cases are recorded in the spring number of Brain for 1900 by Russell, Batten and Collier.

Among 50 cases of pernicious anemia we have had no previous instance of hemiplegia. Thrombotic lesions are well recognized in other forms of severe anemia, as, for instance, in that following post partum hemorrhage and the hemorrhage from gastric ulcer and in chlorosis. (This patient died a few days later. The autopsy confirmed the diagnosis of pernicious anemia. The brain could not be examined.)

#### Exhibition of Gynecological Specimen. DR. HUNNER.

This large ovarian fibroma was removed by Dr. Kelly 12 days ago from a patient now in the ward. I present the

case to emphasize an important point in diagnosis—namely, when a woman presents herself suffering with ascites, you should never overlook the possibility of its being caused by a solid ovarian tumor which *per se* is a benign affliction.

This patient is 53 years of age and has always been a healthy woman up to 12 years ago when she had a very severe attack of abdominal pain in the right side and lumbar region. This attack lasted a week and at times required morphia and even chloroform to ease the pain. She has had two similar attacks since, one two years ago lasting several weeks, and one last October. Ten years ago she was told that she had an abdominal tumor and eight years ago she went to one of the most prominent surgeons of Boston who told her she had a tumor but not to worry about it. A prominent gynecologist of New York to whom she went for five succeeding years gave her the same advice.

Other than these attacks of pain she had no symptoms until the summer of '99 when she began to fail in health and the abdomen began to enlarge. Since the last attack of pain in October, 1901, the ascites has increased very rapidly and she has been tapped five times because of the ascites and consequent dyspnoea.

Her experience with physicians for the past few months makes an interesting and amusing story. She was finally induced to come to Dr. Osler for consultation; he at once recognized her condition and advised operation. The abdomen was greatly distended by free fluid, in which could be palpated a large solid tumor which one could easily push about in the abdomen. Between 8 and 10 litres of ascitic fluid were evacuated and this large tumor was found lying between two systems of blood supply, one from the ovarian pedicle, and the other from the adherent omentum. The tumor with its pedicles had been rotated two and one-half times, causing a great distention of the large veins.

This is the tenth large ovarian fibroma occurring in Dr. Kelly's service at this Hospital in 9400 gynecological admissions. Five of these patients were above 50 years of age, the average age being 48 years. Four of the patients have had very large accumulations of fluid and 4 patients no ascites. I find that in the cases with great ascites there was twist of the pedicle or a subperitoneal development with probable interference with the circulation. Six of the ten patients had an associated myoma of the uterus.

#### DISCUSSION.

DR. OSLER.—I became aware many years ago that solid tumors of the abdomen are sometimes associated with recurring ascites. It must have been in 1885 when returning to Philadelphia from Toronto I was asked to see a lady aged about 36 who was said to be dying. She had been tapped repeatedly and was supposed to have some malignant disease of the peritoneum. I found the woman very much emaciated, with a distended abdomen, and on deep palpation I could feel a very definite tumor that could be moved from side to side. Her condition seemed to war-

rant an operation and it was performed by Dr. Thomas of New York, who removed a solid tumor. The woman is alive and well to-day. The case made a great impression on me and ever since I have been on the lookout for such tumors in cases of ascites of doubtful origin.

This case was interesting too because of the number of diagnoses made and the doubts expressed as to the nature of the case. She had been tapped just before she came to me and I could feel a tumor on the right side which could be pushed over to the left side by ballottement, and was very suggestive of a pedunculated tumor. It is only justice to say of her surgeons that operation was advised, but she was not willing to consent.

#### **Albuminous Expectoration.** DR. ALLEN.

(To appear in the Johns Hopkins Hospital Reports.)

#### **The Relation of Lymphatics to Connective Tissue in the Skin.**

DR. MACCALLUM.

(To appear in a future number.)

*April 21, 1902.*

The meeting was called to order by the President, Dr. Osler.

Dr. Hunner having resigned the Secretaryship, Dr. M. B. Tinker was unanimously elected to the vacancy.

#### **Cases of Malignant Endocarditis with Septicaemia.** DR. COLE.

It is well recognized that clinically two special types of malignant endocarditis occur: first, the so-called septic or pyemic type, and second, the typhoid type. In the latter group of cases, the course is frequently that of a simple continued fever, and not rarely the cardiac condition is entirely obscure. In such cases, cultures made from the blood are frequently of the greatest aid in diagnosis. Such a case is the first one which I wish to report.

The case was that of a young man, aged 23, who was admitted to Ward F, February 16, 1901, a diagnosis of typhoid fever having been made by his physician in attendance before admission. The patient was a teacher in a business college. He had not been injured in any way and had not been exposed to any sort of pyogenic infection so far as could be determined, except that about one month previous to his present illness, following a slight abrasion of the skin, there had been a slight infection at the root of the nail of the middle finger of his left hand. At the time of admission all that was to be seen of this was a very slight scar and reddening of the skin. Two days before admission the patient had been taken ill rather suddenly with general malaise and headache. He had had slight epistaxis and there was a slight eruption of herpes on the lips. He gradually became worse, becoming somewhat irrational on the evening before admission. He was still irrational on entrance. His temperature was 105.2°, pulse 32, leukocytes 10,400. His face was flushed, tongue dry and coated. His

aspect was typhoidal. The examination of the lungs was negative beyond the presence of a few scattered mucous râles, and there were no signs of any cardiac involvement. There were one or two atypical rose spots over the abdomen. Beyond this the examination was practically negative.

All these features made the case appear probably one of typhoid fever. The Widal test, however, was negative.

Blood cultures were made on the following day in the manner used for making blood cultures in typhoid fever; that is, 10 cc. of blood were withdrawn from a superficial vein and added to large amounts of bouillon. After twenty-four hours it was found that in all the culture media, instead of a growth of typhoid bacilli, as was expected, there was a profuse growth of staphylococci. The possibility of this growth being due to a contamination was considered, especially as, when cultivated on agar, it was found that the growth of the organism resembled that of *Staphylococcus pyogenes albus*. Consequently, on the following day a second culture was taken, the result of which was exactly the same as that of the previous one.

As the delirium had persisted and there seemed to be some pain in the neck on attempting to move the head, and also as movements of the arms were resisted, the possibility of the presence of a meningitis was considered, and a lumbar puncture was performed on February 18. The fluid was very slightly cloudy. The centrifugalized sediment showed a few leukocytes and red blood corpuscles. Cultures made from this fluid also gave a pure growth of *Staphylococcus pyogenes albus*.

The further course of the disease much resembled that of an ordinary case of typhoid fever. The temperature became slightly lower after the tenth day and ranged during the entire course of the disease between 102° and 105°, on two or three occasions dropping as low as 101°, and on two occasions reaching 105.5°. The leukocytes ranged between 7,250 and 13,000 until March 3, when they rose to 25,250 and continued high after this time. At no time was there any chill, and sweating was noted only two days before death. After the lumbar puncture the delirium became less, and until three days before death the patient's mental condition was quite bright. The rigidity of the muscles of the neck and arms also became less marked, becoming evident again only on March 5, four days before death.

On February 22 there was noticed a slight swelling and tenderness over the right parotid. The left ankle was also swollen, slightly reddened, painful and hot. The parotid did not suppurate and the swelling and tenderness over it disappeared entirely after three or four days. No suppuration occurred in the ankle joint.

During the entire course of the disease the heart sounds were perfectly clear, the only indication of any cardiac involvement appearing two days before death, when a gallop rhythm was noticed.

Widal tests were made repeatedly during the course of the disease, but on each occasion the result was entirely negative.

Blood cultures were made on six different occasions. On February 17 and 19, the cultures were made only in liquid media and the number of organisms could not be determined. The later cultures were made in agar plates as well as liquid media, and so the number of organisms in each cc. of blood could be estimated. The following are the results obtained:

February 21,	No. of organisms,	8 in 1 cc. of blood.
" 25,	" "	6 " "
March 1,	" "	30 " "
" 7,	" "	230 " "
March 9 (autopsy),	" "	10,000 " "

It will thus be seen that there was a marked and gradual increase of the number of organisms in the blood during the course of the disease.

Cultures were made from the urine on three different occasions, a pure culture of *Staphylococcus pyogenes albus* being obtained each time.

February 18—Cocci present in small numbers.

February 23—50 colonies grew from 1 loopful of urine.

March 3—200 colonies grew from 1 loopful of urine.

The virulence of the organism isolated from the blood was tested by injection into animals. It proved to be of very slight virulence for rabbits. 4 cc. of a forty-eight hour bouillon culture were inoculated into the ear vein of one rabbit. It continued well for ten days, then 4 cc. more of a forty-eight hour culture were inoculated into the same animal. This rabbit died twenty days after the first inoculation, apparently from toxæmia. There were no abscesses and the organism could not be recovered from any of the organs. A similar result was obtained from a second rabbit. A guinea-pig, inoculated intraperitoneally with 3 cc. of a seventy-two hour culture, died after three days. At autopsy an abscess was found in the kidney, from which *Staphylococcus albus* was isolated.

From March 7 to March 9 the patient's condition grew gradually worse, gallop rhythm persisted; there was active delirium and also marked rigidity of the muscles of the arms. Death occurred on the morning of March 9, on the twenty-fourth day of disease.

An autopsy was performed on the same day.

Anatomical diagnosis: Diphtheritic colitis; acute vegetative mitral-endocarditis; septic infarct of the spleen; abscess in the right kidney; acute hæmorrhagic nephritis; acute splenic tumor; abscess in the ilium; oedema of lungs; chronic proliferative pleuritis; fatty degeneration of the intima of the aorta.

Unfortunately, no examination of the brain and cord could be made.

The bacteriological report of the cultures made at autopsy is as follows:

From the heart's blood, splenic infarct, kidney, liver, and vegetations on mitral valve—*Staphylococcus albus*; from the liver and intestines—*Bacillus lactis aerogenes*.

This case, then, represents a characteristic example of a

cryptogenetic septicaemia with endocarditis, the main clinical features of which were the continued regular fever, the absence of chills and sweating, the mild degree of leukocytosis, and the absence of any features or signs pointing to any cardiac involvement. Except for the results obtained by blood cultures, this case would undoubtedly, for some time at least, have been considered one of typhoid fever. Therefore, too much stress cannot be laid on the value of a bacteriological examination of the blood in all cases of fever, the nature of which appears at all doubtful.

The second case was one also of acute endocarditis and septicaemia; this case, however, not running so typically a typhoidal course as the former. In this case the source of infection could be directly traced to a miscarriage which occurred about a month before entrance.

The case was that of a woman aged 28, who was admitted to the gynecological service on April 2, with the diagnosis made before admission, of renal abscess. On examination no localizing features could be made out and operation was considered inadvisable, so she was transferred to the medical service.

She gave a history of being seized suddenly on March 2, one month before admission, with pains in the abdomen. At this time she was in the fifth month of pregnancy. Associated with the pains were chilly sensations and frequent micturition. Three days later the membranes ruptured and the labor pains became more severe. They continued for two days, when the patient became exhausted, and manual delivery was undertaken by her physician and the child was delivered, the placenta being delivered first. There was very little hemorrhage and there did not seem to be much shock following the operation. She continued having fever, however, and losing weight, and gradually increasing pallor was noticed. She had nine shaking chills before admission to the Hospital, her temperature, according to the history, having once reached 108°. Associated with the chills there was marked sweating.

The patient seemed very ill on admission. The temperature was 101.5°, pulse 152, respiration 32. There was no abdominal pain. The urine was quite normal. On the day after admission the patient's temperature fell to 95.5° and then rose within six hours to 106.4°. This sudden rise was accompanied by a severe shaking chill. Examination of the blood on admission showed a considerable degree of anaemia; red blood corpuscles, 2,208,000; hemoglobin, 30 per cent; leukocytes, 13,000. Examination of the heart showed that over the precordia above the fourth rib there was audible a very intense and rough systolic murmur, of maximum intensity over the sternum opposite the third rib, also heard in the second left interspace. On the following day there was heard over the sternum what was thought to be a very soft pericardial friction rub. This persisted throughout the entire course of the disease, while signs of endocardial involvement become no more definite, but rather less marked than on admission; so that there was thought to be present a

pericarditis, while the existence of endocarditis was considered doubtful. While the pulse was weak and rapid, it continued perfectly regular.

After the chill on the day after admission the patient's temperature continued constantly between 101.5° and 105°, never falling to normal. There were no chills and there was no sweating. The temperature curve after the sudden rise above noted resembles one of typhoid fever, the variations being of slight extent.

On April 8 signs of consolidation of the lower lobe of the right lung appeared. These signs gradually became more marked. The patient had very little cough, however, and no shortness of breath. She grew gradually weaker and weaker until death occurred on April 14, twelve days after admission.

Autopsy was performed by Dr. MacCallum.

Anatomical diagnosis: Puerperal condition of uterus after abortion. Parametritis. Suppurative thromboses of vessels in the broad ligament; thromboses of femoral and iliac veins. Vegetative tricuspid endocarditis. Embolism of pulmonary artery on right side. Multiple pulmonary infarctions. Fibrinous purulent pleuritis. Acute splenic tumor. Parenchymatous degeneration of other viscera.

The condition found in the heart was very remarkable, and on account of the size of the vegetations on the tricuspid valve the condition resembled that seen in the specimens of gonorrhoeal endocarditis. The following note on the heart was made by Dr. MacCallum:

"Heart.—Weights 250 grams, is not enlarged. The right auricle contains soft clots. On opening the right auricle the tricuspid orifice is found to be completely shut off by three masses of whitish vegetations which can be separated by stretching the valvular orifice; the maximum opening thus produced is only about 4 mm. in width. The ventricular surfaces of the valve are almost smooth, being covered here and there only with vegetations. The papillary muscle similarly shows very few vegetations, but one or two smaller branches of the papillary muscle are broken as if vegetations had existed. Large nodular masses of almost uniform yellowish white color enter the auricular side of the tricuspid valve. The left auricle contains only soft clots. The mitral valves are not abnormal. The aortic and pulmonary valves are delicate and competent. The coronary arteries are smooth. The myocardium is rather pale and flabby. The greyish pink muscle is flecked with many spots of paler grey."

While from the clinical features of this case the diagnosis of a septicæmic condition was fairly definite, yet the physical examination did not reveal any definite signs of any local lesion, though, as above stated, it was thought possible that a pericarditis existed.

Cultures were made from the blood on April 4 (the second day after admission) by the usual methods, and in addition to cultures made in bouillon, agar plates were also made, one cubic centimeter of blood being introduced into each plate. In the bouillon after twenty-four hours

a coccus growing in chains was found, and there had also developed on the plates fine pin-point, dewdrop-like colonies, smears from which also showed cocci growing in chains. The diagnosis of streptococcus septicæmia was made and the patient was given antistreptococcus serum on four successive days. This treatment, however, seemed to have no influence on the course of the disease. Cultures were made from the blood on three occasions and the number of colonies grown in the plates were counted with the following results:

April 4, No. of organisms,	480 to 1 cc. of blood,
" 8, " "	3,642 " "
" 12, " "	10,716 " "

On transferring the organisms from the original cultures, which, of course, contained a considerable amount of blood, to ordinary culture media, such as agar, it was found that no growth occurred; while, when transferred to hydrocele agar a good growth of small colonies, made up of cocci, frequently appearing as biscuit-shaped diplococci arranged in chains, occurred. The possibility of the organism being gonococcus was at first considered. However, after repeatedly transferring the organism it was made to grow quite well on plain agar, in litmus milk, and in bouillon; in all cultures a characteristic growth of *Streptococcus pyogenes* being obtained.

The pathogenicity of the organism was tested by the inoculation of 1½ cc. of a twenty-four hour culture into the peritoneal cavity of a rabbit. The rabbit died after forty-eight hours. No macroscopical foci of infection were discovered, but streptococci were obtained in cultures made from the heart's blood, spleen, liver, and kidney.

Cultures were also made from the patient's urine on April 13, and it was found that the urine contained streptococci in very large numbers.

The following are results of the cultures made at autopsy by Dr. Harris:

From the heart's blood, vegetations on tricuspid valve, abscess of lung, pleura, pericardium, kidney, thrombus in left femoral vein, and uterine cavity—*Streptococcus pyogenes*; from the uterine cavity—*Bacillus coli*.

Cover slips made from the various organs, including the vegetations on the tricuspid valve, showed diplococci and streptococci, staining by Gram. No organisms resembling gonococci were found.

The blood changes in this case are of considerable interest:

First, the leukocytes on admission were low, 6000, and remained between this and 13,000, counts being made every day. Probably this moderate leukocytosis should be considered as due to the extremely severe infection, and also to poor resistance on the part of the patient.

Second, the anaemia which was noted on admission increased rapidly before death. On April 9 the red blood count had fallen to 1,684,000, haemoglobin 28 per cent; while on the day of death the count was red blood corpuscles 1,352,000, haemoglobin 32 per cent.

This extreme and rapidly progressive anaemia in acute streptococcus infection has been noted especially by Grawitz, who states that according to Rocher's investigations, "It is probable that the diminution of red cells in septicaemia is greater than in any other infective disease and appears in a shorter time." Grawitz reports a case in which the red blood corpuscles fell to 300,000 per cubic centimeter. In this case, however, there had been marked uterine hemorrhage.

In this connection attention should be drawn to the work of Besredka,<sup>1</sup> which has just appeared, on the streptococcus haemolysine. It stated that *Streptococcus pyogenes* is the only organism, to the author's knowledge, which when injected into an animal is capable of causing haemolysis. In this it differs essentially from all other bacteria, as they exercise haemolytic power only *in vitro* and never *in vivo*. According to his work the haemolytic substance is intimately associated with the body of the bacterium and is not found in the filtrate of a culture. This appears to give a rational basis for the marked anaemia occurring in general streptococcus infections.

#### DISCUSSION.

DR. OSLER.—There are one or two points about these cases to which I would like to refer. In the first place the absence of murmurs in the first case. I examined the heart on eight or ten occasions and I can speak positively of the normal character of the sounds. He had no murmur throughout the course and in fact it is remarkable to see a man with such a high fever without even a haemic bruit. I have reported cases of extensive endocarditis in which no murmur was present. In the second case, at the height of the fever, there was for several days over the mid-sternum a very remarkable murmur, superficial, rough, double, intensified by pressure and with the character of a pericardial bruit. It did not extend to the left nor to the right and it diminished in intensity after persisting for several days.

Another point of interest in the first case was the very slight injury which, though occurring a month before, was, I think, undoubtedly the seat of infection. A third point of special interest is the occurrence of profound anaemia in these cases of septicaemia. Some of you will call to mind the fact that in at least two of our cases of gonorrhoeal endocarditis the question of pernicious anaemia was raised at the time of admission.

#### Exhibition of Specimen. DR. MACCALLUM.

The heart from the second case reported by Dr. Cole was exhibited. The autopsy in this case revealed the existence of a well defined parametritis, the broad ligament on the left side being very much thickened and indurated. On section the tissue appeared very oedematous and flecked with opaque patches of fibrin. From the blood vessels greenish pus could be expressed.

The organs were extremely anaemic, and from the fact that in cultures made with blood mixed with agar a clear halo surrounded each colony of streptococci, it seems probable that the anaemia might be due to the haemolytic action of the poisons produced by the streptococcus.

There was also a remarkable vegetative endocarditis in which the tricuspid valves only were affected, the orifice being practically occluded with the exception of a narrow slit. The great size and firmness of the vegetations as well as their unusual situation suggested that they might be due to infection with the gonococcus, but in all smears and cultures the streptococcus described was found unmixed with any other organism.

There was no pericarditis.

#### Note on a Case of Infection by *Bacillus Aerogenes Capsulatus*, in which the Organism was Demonstrated in the Circulating Blood during Life. DR. COLE.

(See October BULLETIN, 1902, page 234.)

#### Observations upon Recent Methods of Treating Corneal Ulcers. DR. THEOBALD.

(See Amer. Jour. of the Med. Sciences, June, 1902.)

#### DISCUSSION.

DR. SLACK.—I have enjoyed Dr. Theobald's paper very much. I have employed carbolic acid in this way in my practice for a good many years. I first saw it used by Dr. Casey Wood, who applied it, however, with a simple wooden toothpick without any cotton attached. If the patient happens to be an inquisitive one I find it an advantage to tell them I am applying phenol, since so many people nowadays have a fear of carbolic acid because of the numerous fatal poisoning cases published in the daily press.

Monday, May 5, 1902.

Meeting called to order by the President, Dr. Osler.

#### The Quantitative Estimation of Uric Acid by the Permanganate Method. DR. BAUMGARTEN.

(To appear in a future number.)

#### DISCUSSION.

DR. EMERSON.—The work of Dr. Baumgarten has been most interesting to us of the clinical laboratory as it throws considerable doubt on any permanganate method. That may not be grateful news to a good many. They have accused uric acid of everything possible, thirty-nine ailments being attributed to it and lately an oculist has come forward with the statement that many cases of astigmatism against the rule are probably due to this agent. The presence of uric acid has been determined without doubt in most cases by the permanganate method, if it has been determined at all, because the Salkowski method is beyond the use of most men. It should be said, however, that this method has never been recognized as totally beyond criticism. Some of

<sup>1</sup> Ann. de l'Inst. Pasteur, Dec., 1901.

the best authorities do not even mention it in their works, while others say that perhaps good clinical results may be obtained by it but the most accurate results can not. The work of Dr. Baumgarten has shown the correctness of this statement.

#### **Exhibition of Patients. DR. GILCHRIST.**

CASE 1.—This patient came to the dispensary two days ago with a bullous eruption of the extremities, especially of the hands and feet. The father called my attention to the fact that the child had been in the dispensary two or three years ago. The patient is a boy six years old. The disease is a very rare one and only seven or eight cases have been recorded in this country. It was first described about twenty years ago by Goldscheider in Germany. It is a distinctly hereditary disease, always of a bullous character and generally attacks the extremities or parts of the body where there is much friction. The disease has been given the name of *Epidermolysis Bullosa Hereditaria*. Some observers have found the disease running through three generations and in one instance to even the fifth generation. It commences soon after birth, is always worse in the summer and begins as a small clear bulla which rapidly increases in size. In this patient the disease made its first appearance on the fourth or fifth day after birth. The father says that three other children, all of whom are dead, had the same disease. The boy resembles his mother, who had the disease as did also her father. One of the children lived only a few days, but had a bullous eruption; a second child, suffering from a similar skin disease, lived two years and died of marasmus. This patient is the third child, and the fourth, a girl, also had the disease but died in infancy. I followed the present case for two and a half years ('98-'00) and noticed that during the winter he always enjoyed very good health but with the first onset of warm weather the bullous lesions appeared on the hands and feet.

There is no regularity about these lesions. The first case of this disease which I had the opportunity of seeing occurred in a woman forty-five years of age who could always produce such a blister by simple friction, as tying a garter too tightly. The patient consulted me in my office and at my suggestion she tied a knot in her garter, went out for a walk for half an hour and on reappearing at my office I saw quite an extensive bulla, produced by friction with the knot. Cultures from this bulla were sterile. Smears showed a few eosinophiles. Dr. Harry Lee Smith of this city has published a case, the first to be recorded in the colored race. Elliot of New York was the first to show that in this disease the deepest layer of the epidermal cells did not present a normal appearance even in the apparently normal skin of these patients, and he proved that the vesicle forms in this layer.

The histological findings of Elliott seem to oppose the theory with which we are all familiar, that all the other cells of the epidermis are derived from the deepest layer. One can hardly believe the healthy looking superficial cells here are

derived from the apparently abnormal deeper cells. The observations of Elliot were confirmed in one of my cases, namely, the mother of this patient.

Dr. Thomas Brown examined the blood of Dr. Smith's case and found a slight increase of the eosinophiles, and this agrees with the work of Columbini, who has investigated this disease very thoroughly, and of other investigators.

CASE 2.—This patient, a colored woman, shows a very interesting growth on the upper lip, which, when she first appeared in the dispensary two years ago, looked very much like the papillomatous form of tuberculosis cutis. I excised one of the small nodules, which was situated near the large patch, and found no tubercular arrangement but it reminded me more of a syphilitic nodule. I began to treat her for syphilis and within two days she developed the typical papular eruption on the extremities, of that disease. She got practically well after three months' treatment and left us. She stopped taking any more medicine and now returns with a relapse. The whole upper lip is now involved. There appears to be quite an extensive deposit. The margin of the patch is very much raised, very firm, distinctly papillomatous or even warty in appearance. Pus can be squeezed out from between the papillæ. On the margin of the lip on the right half there is some ulceration. The central portion of the whole lip is much smoother and has the appearance of a scar. Sections taken from the margin show the characters of a gummatous deposit, viz., large numbers of giant cells as well as lymphoid cells, but there was no special arrangement in the form of tubercles. No tubercle bacilli were found in the sections.

NOTE.—Since this case was exhibited, the patient has been taking treatment for syphilis for two months and the lesion is rapidly softening and disappearing.

#### **The Origin and Early Development of the Lymphatic System.**

DR. SABIN.

(See *The American Journal of Anatomy*, Vol. I, No. 3, p. 367.)

#### **DISCUSSION.**

DR. OSLER.—I am sure we all congratulate Dr. Sabin on this most brilliant piece of work. One can not but feel a slight regret that notice could not have been sent to Eustachius and the two Hunters, particularly John, who would have been delighted to listen to this demonstration.

*Monday, May 19, 1902.*

The meeting was called to order by Dr. Welch.

#### **An Improved Method of Uretero-vesical Anastomosis. DR. HUNNER.**

I wish to make a brief preliminary report on a method of ureterovesical anastomosis which presents some new features and which I have used successfully on two patients. The great difficulty in anchoring the ureter to the bladder is to find a suture that will resist traction. I was led to experi-

ment upon cadavers after seeing a failure in a ureterovesical anastomosis.

This preserved specimen will serve to demonstrate the method. A working incision from two to three centimeters in length is made in the fundus of the bladder. Choosing the point where one wishes the ureter to enter the bladder a small opening is here made by introducing a scalpel through the working incision and quickly pushing the blade through the bladder wall from within. The lower end of the ureter is now split for one centimeter, thus making two lateral flaps. Two toothed mosquito artery clamps are passed through the working incision and out through the small anastomosis opening and made to grasp the lateral flaps of the ureter. Before drawing the ureter into the bladder by means of these forceps, two silk mattress sutures are taken, one posteriorly and one anteriorly, through the bladder wall near the anastomosis opening, and through the ureteral wall five millimeters above the split. On tying these sutures the ureter is firmly fastened in the wall of the bladder, and we still have the two lateral flaps to be fastened against the bladder wall on the inside.

The two silk sutures already described penetrate only serosa and musciosa. The two sutures which fasten the lateral flaps to the bladder wall penetrate all coats of both the flaps and the bladder. They are of either silk or catgut. If of silk they must be tied within the bladder and cut with long ends so the loops may be removed later through the cystoscope. If of catgut they may be tied either outside or within the bladder and the ends cut short. Before suturing the flaps to the bladder wall the serosa of the flaps and the mucosa of the bladder under the site of the flaps may be denuded, thus apposing muscle surfaces.

The working incision is now closed by the use of silk or catgut, and the questions of subperitoneal treatment and drainage are settled according to the nature of the case.

Thus, by the use of four sutures, we have a comparatively simple and the most secure suture I have yet seen proposed. I have applied the method on two cadavers, two dogs, and two patients and in a later communication I will make a more extended report.

#### **The Differential Lencocyte Count in the New-Born.** DR. WARFIELD.

(See American Medicine, September 20, 1902, p. 457.)

*Monday, June 2, 1902.*

The meeting was called to order by Dr. Hurd.

#### **Nitrogen Excretion in Pneumonia and its Relation to Resolution.** DR. COOK.

(See November BULLETIN, 1902.)

#### **DISCUSSION.**

DR. EMERSON.—During the past few years ferments have attracted considerable attention and our knowledge of them has increased to a marked degree. It is only within the past

three years that Hofmeister's pupils have shown that pepsin is a much more potent enzyme than was formerly suspected. It is only since twelve months or so that Volhard demonstrated in the gastric juice an unsuspected fat splitting ferment. It is scarcely one year since Cohnheim demonstrated in the intestinal mucosa a new ferment which bids fair to prove itself to be more important in digestion than the others combined. Recently the autolytic ferments have proven themselves to be very important in physiological and pathological processes, and of these the one under consideration this evening is perhaps the most interesting. Since Müller's work we know better how the solid pneumonic lung becomes clear: the exudate is digested as if it were a piece of meat in the intestine. We know something of the nature of the ferment, for Müller has shown that the end products of this digestion are many of them the same as in tryptic digestion; we know that the ferment is not the same as trypsin for it acts in acid medium. We can now measure the amount of exudate resolved during the past few hours, for one of Müller's students has shown that to be possible by determining the nitrogen increase in the urine; we now know the curve of nitrogen excretion in various forms of pneumonia, for Dr. Cook has determined this for us.

But the point of greatest interest in Dr. Cook's work is the curve in cases of delayed resolution, for to explain the extraordinary nitrogen output in such cases one would suspect two or three lungs had resolved.

Whether or not Dr. Cook's explanation will stand the test of future work or not remains to be seen. At present, so far as I can see, there is no other to give. It may be hard to think of a continuous inflammatory exudation going on in such cases, but no harder than to imagine the exudate remaining unchanged for several weeks with the identical fibrin strands and the identical pus cells. However this may be the curve of nitrogen excretion in such cases is remarkable, and its true explanation may throw some new light on the pneumonic processes.

#### **The Metabolism in Albuminuria.** DR. EMERSON.

(To appear in Vol. X of The Johns Hopkins Hospital Reports.)

#### **Actinomycosis.** DR. ERVING.

(See November BULLETIN, 1902.)

#### **The Clinical Value of Oliver's Hæmocytometer.** DR. BAUMGARTEN.

(See July BULLETIN, 1902, page 176.)

#### **DISCUSSION.**

DR. EMERSON.—In considering the value of Oliver's Hæmocytometer it should be born in mind that it was not introduced as a short cut to blood counting, an easy clinical method for obtaining approximate results. Oliver found that the Thoma Zeiss counter did not give results accurate enough for his physiological experiments and invented this

as a more accurate instrument, a superior method for counting red blood cells of normal blood.

The question will be asked at once, how can a blood count be made more accurately than by counting the cells? And the answer is this: by blood count is meant the result calculated from the average number of cells in eight of the sixteen unit squares of the millimeter square. As a rule I am afraid the term "blood count" means the result of less work than this. Now if the person counting has patience enough to count many more squares than this his result will be much more accurate, and this is what Oliver did in standardizing his instrument. He counted one hundred and twenty squares. With an instrument thus standardized the results obtained are more accurate than the ordinary blood counting and much easier, but its greater accuracy is the essential thing, providing the blood be normal, and it is the slight physiological variations one is studying. Oliver expressly stated that his instrument should not be used in blood diseases. But the ease and rapidity with which the instrument is used of course won it favor, and it has been

recommended for clinical work. One person compared it with actual counting in twenty-seven cases, including various blood diseases, and obtained results which compared wonderfully. I do not believe two persons each with Thoma Zeiss instruments would have done much better, if as well.

We have used the instrument in the clinical laboratory. So long as the blood was normal the results were strikingly constant, but in chlorosis and pernicious anemia, far from accurate. Dr. Baumgarten has carefully gone over this work. He finds that the plasma is precipitated by Hayem's solution and that this is an important source of error in low counts. He finds also that the size of the corpuscles is a matter of considerable importance, large corpuscles giving a high count, small corpuscles a count too low. By correcting these errors the results compare more favorably with the actual count, but even then not well. How Scannell got such satisfactory results in cases of primary anemias without making corrections for either source of error we are at a loss to explain.

## NOTES ON NEW BOOKS.

**Minor Surgery and Bandaging**, including the treatment of fractures and dislocations, the ligation of arteries, amputations, excisions and resections, intestinal anastomosis, operations upon nerves and tendons, tracheotomy, etc. By HENRY R. WHARTON, M.D., Professor of Clinical Surgery in the Woman's Medical College of Pennsylvania, etc. Fifth edition, enlarged and thoroughly revised, with 509 illustrations. (Philadelphia and New York: Lea Brothers & Co., 1902.)

This is an excellent book for students and well deserves the success which is emphasized by the fact that it has reached its fifth edition. The important subject of surgical bacteriology in the present edition has a special chapter devoted to it. The book is well printed and fully illustrated.

**A Text-Book of Surgery.** By Dr. HERMANN TILLMANN, Professor in the University of Leipsic. Translated from the Seventh German Edition by BENJAMIN T. TILTON, M.D., Instructor in Surgery, Cornell University, and JOHN ROGERS, M.D., Instructor in Surgery, Cornell University. Edited by LEWIS A. STIMSON, M.D., Professor of Surgery, Cornell University. Volume I—The principles of surgery and surgical pathology. With five hundred and sixteen illustrations. (New York: D. Appleton & Company, 1901.)

This work is a thorough revision of the translation of the third German edition which appeared in 1894 and which was extensively used in medical schools. The great advances which have been made during seven years in pathology and bacteriology have practically made the present edition a wholly new book. The translation seems very well made. We regret to see mistakes in the spelling of some well-known American names however.

**American Edition of Nothnagel's Encyclopedia.** Diphtheria. By WM. P. NORTHRUP, M.D., of New York. Measles, Scarlet Fever, and German Measles. By Professor Dr. TH. VON JÜRGENSEN, Professor of Medicine in the University of

Tübingen. Edited, with additions, by WILLIAM P. NORTHRUP, M.D., Professor of Pediatrics in the University and Bellevue Medical College, New York. Handsome octavo, 672 pages, illustrated, including 24 full-page plates, 3 of them in colors. Cloth, \$5.00 net; Half Morocco, \$6.00 net. (Philadelphia and London: W. B. Saunders & Co., 1902.)

This volume, the third in the series of English translations of the "Nothnagel System of Practical Medicine," is fully equal to its predecessors. The article on Diphtheria, entirely original with the editor, is fully in keeping with the high standard set by the other German articles which comprise the work. Dr. Northrup was associated with Dr. O'Dwyer at every step in the perfection of intubation tubes and is particularly fitted to describe this aspect of the treatment of diphtheria.

Professor Jürgensen's monograph on Measles is one of the most comprehensive contributions on that infection which has appeared and brings out fully the valuable Danish records of the Faroe Islands epidemic. His exposition of Scarlatina is unrivaled both for clinical detail and exactness and clearness of statement. "Fourth Disease" and German Measles are also treated of briefly. The book is profusely illustrated, containing, besides a large number of text cuts, twenty-four full-page plates, three of which are in colors. The illustration of Koplik's sign is very good.

**Diseases of the Nose, Pharynx, and Ear.** By HENRY GRADLE, M.D., Professor of Ophthalmology and Otology, Northwestern University Medical School, Chicago. Octavo of 547 pages, profusely illustrated, including two full-page plates in colors. (Philadelphia and London: W. B. Saunders & Co., 1902.)

This volume is intended to present diseases of the Nose, Pharynx, and Ear as the author has seen them during an experience of nearly twenty-five years. The result is an eminently practical and helpful book which can be commended to students. The text is concise, the illustrations are good and the therapeutic suggestions are sensible.

Transactions of the Chicago Pathological Society. From October, 1899, to June, 1901. Volume IV. (Chicago: American Medical Association Press, 1902.)

This volume is most creditable in contents, illustrations and press-work. We congratulate the Chicago Pathological Society upon the character of its scientific work and its mode of presentation to the public. It is to be hoped that eventually full stenographic reports may be published of the communications and discussions at the regular meetings.

The Operations of Surgery. By W. H. A. JACOBSON, M. Ch. Oxon., F. R. C. S., Surgeon to Guy's Hospital; Consulting Surgeon Royal Hospital for Children and Women; Member Court of Examiners Royal College of Surgeons, etc.; and F. J. STEWARD, M. S. London, F. R. C. S., Assistant Surgeon Guy's Hospital and to the Hospital for Sick Children; Surgeon in Charge of the Throat Department, Guy's Hospital. Fourth Edition, Revised, Enlarged and Improved. 550 Illustrations. Two Volumes: Volume I—Operations on the Upper Extremity; Operations on the Head and Neck; Operations on the Thorax. Volume II—Operations on the Abdomen; Operations on the Lower Extremity; Operations on the Vertebral Column. (Philadelphia: P. Blakiston's Son & Co., 1902.)

It is stated upon the title page that this treatise is intended especially for the use of those recently appointed to hospital positions and for those preparing for the higher examinations. It is, however, of the highest utility to all surgeons and the authors deserve much praise for the comprehensive character of the work. Although an English book, full credit is given to many American surgeons. Thus, for example, Tiffany and Keen's work on the Gasserian ganglion is fully described; Halsted's breast and hernia operations; McBurney's operations for hernia and appendicitis; and special operations of Nancrede, Kelly, Bryant, Finney, Fenger, Senn, M. H. Richardson, Walker and others. Nothing impresses one more than the catholicity of the book in its dealing with surgeons of every land. It is doubtless possible to point out defects of method and faults of execution in so large a work but we have no disposition to do so since the results of the volumes themselves are so large. The declaration of the authors that the present work must be rewritten from time to time is after all the surest guarantee of the continued success of the book. Edition must follow edition and methods at present in vogue must be modified or rejected as farther knowledge is acquired. The present edition is creditable in every way and can but be most helpful to those for whose benefit it has been prepared.

Quain's Dictionary of Medicine. By various writers. Third edition largely rewritten and revised throughout with fourteen colored plates and numerous other illustrations. Edited by H. MONTAGUE MURRAY, M. D., F. R. C. P., Joint Lecturer on Medicine, Charing Cross Hospital, etc. Assisted by JOHN HAROLD, M. B., Physician to St. John and St. Elizabeth's Hospital, etc., and W. CECIL BOSANQUET, M. D., Physician to Out-Patients, Victoria Hospital for Children, Chelsea, etc. (New York: D. Appleton & Company, 1902.)

Those who were much disappointed in the second edition of Quain's Dictionary can congratulate themselves that the work of preparing the third edition has fallen into such competent hands. Much which had become obsolete in former editions has been omitted and many details as to modern discoveries have been added. In articles like those on malarial fever, diphtheria, typhoid fever, diseases of the pancreas, angina pectoris, morbid conditions of the blood, one feels that the present state of medical knowledge has been carefully reflected and nothing remains to be added. The work is a single volume of about 1900 pages and is easy of reference. The colored illustrations are good and the press work and paper are excellent. The book is worthy of a place in every good library.

The Medical Annual. A Year Book of Treatment and Practitioner's Index. 1902. (Bristol: John Wright & Co.; New York: E. B. Treat & Co.)

This is the twentieth year of this annual and those who have used it know how valuable it is. As the title suggests, special attention is given to treatment and there is a considerable section on new drugs and procedures in therapeutics. The subjects are arranged in alphabetical order and to certain ones special attention has been given. Thus, in the article on arsenical poisoning by Dr. Kelynack, the circumstances of the recent epidemic in England have been well summarized and the principal features pointed out. The literature is given and the article is illustrated by two excellent plates of the skin lesions. Under the heading of aseptic surgery is a good description of some of the New York operating rooms and the general methods employed. The articles throughout are well done; it is of course impossible to note them in detail. There are sections on sanitation and on recent medico-legal decisions. A list is given of the principal medical works published during the year. Altogether this work is very helpful and worthy of commendation.

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# BULLETIN

## OF

# THE JOHNS HOPKINS HOSPITAL

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## ACTINOMYCOSIS HOMINIS IN AMERICA, WITH REPORT OF SIX CASES.<sup>1</sup>

WILLIAM G. ERVING, M. D.

The first cases of actinomycosis hominis to be noted in America were those reported by Murphy of Chicago in 1885. Seven years previously the articles of Bollinger, Harz, and Israel, appearing in Germany, had definitely established the relationship of the disease in animals and man to its cause—the streptothrix actinomycotica, or ray fungus.

In the years subsequent to the appearance of Murphy's article, numerous cases of the disease were reported from various parts of this country, until, in 1899, Dr. John Ruhräh of Baltimore was able to present a collection of 58 cases, many of which were then published for the first time.

In this most thorough discussion of the subject, the results obtained from a compilation of these American cases were compared with those of several hundred cases collected in Europe by Moosbrugger, Sokolow, Guder, Poncet and Bérard, and others, to bring out many valuable facts regarding the disease and its treatment.

To this collection Ruhräh subsequently added 4 cases as addenda, and seven others in a supplementary report appearing in 1900, thus including all the cases appearing in the American medical literature to November, 1899.

Since the publication of Ruhräh's article, cases have been more frequently reported, 25 appearing in the current American literature from November, 1899, to December, 1901, inclusive.

In addition to these, five cases occurring in the wards of the Johns Hopkins Hospital and a sixth in those of the Union Protestant Infirmary of Baltimore are now reported for the first time, making a total of 100 American cases.

Of the five cases observed in this hospital—all of which have occurred within the past three years—the disease was primary in the cervico-facial region in one, in the thoracic region in a second, and in the abdominal region in the remaining three. One of the abdominal cases died and one recovered, while the other cases have not yet been discharged. The sixth case, where the disease was located in the abdominal region, terminated fatally.

Following are the chief points in the clinical histories of each:

*Case No. 1.*—A. B., male, black, 17 years old, a rivet cleaner, from Hampton, Va.

He entered the hospital September 24, 1901, complaining of pain in the right side of face.

There was nothing of importance in his family or personal history, nor any history of infection. Eight months previous he first noticed stiffness of the lower jaw and swelling in front of and below the right ear.

This swelling increased slowly, became painful, and in April he was operated on at the Hampton hospital, and the pain was relieved, but discharging sinuses persisted in the wound.

Examination showed a large swelling in the region of the

<sup>1</sup> Read before the Johns Hopkins Hospital Medical Society, June 2, 1902.

zygoma and under the ramus of the jaw, soft and tender, save below the ear where there was a hard mass. He was unable to separate his jaws. Numerous sinuses were present, containing typical "sulphur" granules, in which the ray fungus was demonstrated microscopically. The febrile response to the administration of tuberculin was somewhat suggestive, not typical.

For two months the patient's condition remained the same, new sinuses appearing at intervals and his temperature ranging from 99°-100° F., while blood examinations showed a moderate leucocytosis of 8-10,000. On November 16 Dr. Mitchell explored the region of the right lower jaw, which was found to be greatly thickened, due to the formation of spongy tissue beneath the periosteum. This was chiseled away to normal bone, the adjacent diseased soft parts and scar tissue were dissected out, and the wound was packed with iodoform gauze. The after-treatment consisted of irrigations, at first daily, then on alternate days, with weak bichloride of mercury solutions, and the draining of the wound with iodoform gauze, for which last, gauze soaked in a saturated solution of potassium iodide was substituted in January and continued three months. At the same time KI was administered internally in increasing doses, reaching a maximum of 50 grains t. i. d. The wound healed slowly until early in March, when but a single sinus remained. However, at intervals the right side of face would swell and the patient would suffer considerable pain. These conditions grew worse and in March a new sinus appeared under the ramus, admitting a probe a distance of 5 cm.

On March 27 Dr. Mitchell again explored the jaw, found that the new sinus extended nearly to the coronoid process, while, communicating with the old sinus in the region of the zygoma, was a pocket containing about 10 grams of pus. He removed the coronoid, part of the zygoma, and much of the ramus, and dissected away the granulation and scar tissue, this last permitting the jaws to be widely separated. The after treatment was similar to that following the first operation, and the wound is healing slowly, while the patient's general condition remains good.

*Case No. 2.*—J. B., male, white, unmarried, age 26 years; residence, Mt. Wolf (York Co.), Pennsylvania; occupation, farmer.

Entered the Johns Hopkins Hospital September 24, 1901, complaining of a discharging sinus in the chest.

His family and personal history was unimportant. In March, 1901, he began to suffer from fever and pain in the chest. His chest bulged and his heart was displaced. Was needled several times and finally pus was obtained in the left lower back. An incision was made and considerable pus was evacuated. There has been an intermittent discharge ever since.

One week before admission a red and tender swelling appeared on the left side of chest, outside and below nipple. This was opened a few days before admission, and a small

amount of pus was evacuated. There had been considerable loss of weight in the past six months, largely regained of late.

Examination disclosed a red swollen area, a hand's breadth in diameter, its center in the left anterior axillary line, which was very tender on palpation. Pus escaped from a sinus admitting a probe as far as the rib. Below the angle of the left scapula in the seventh interspace was a sinus discharging pus freely. There was decided flattening and impaired motion of the left side of chest. Distinct flatness and absence of breath sounds and vocal fremitus were found over entire lower left chest.

On September 26 Dr. Follis excised the posterior sinus, removed 4 cm. of the 8th rib, and opened into a cavity 18 x 15 cm. which contained a large amount of thick yellow pus. In this a branching bacillus was found, which did not grow upon ordinary media. The cavity was packed with iodoform gauze and a drainage tube inserted. The abscess over the same rib anteriorly was also opened and curetted out. There was seemingly a communication between the two cavities.

For two months the patient's condition was improved but a copious discharge continued.

About the middle of November a swelling 6 x 8 cm. appeared outside and below the anterior wound, painful and tender, and presently fluctuating. On November 25 Dr. Follis incised this, evacuated some pus, curetted and swabbed with carbolic the soft parts and the other sinuses, removed a portion of the involved rib, spongy in character, and irrigated the posterior cavity with salt solution.

In the pus were found typical "sulphur" granules, containing the ray fungus.

KI was administered internally in increasing doses to 30 grains t. i. d.

The patient's condition improved, his temperature remained normal, the wounds slowly granulated up, and he was discharged on December 20, with orders to continue the KI treatment and to return in two months if the sinuses persisted.

On February 4 he returned. In the middle of January the sinuses had closed and 10 days later a swelling appeared over the spot, associated with fever and chills. This was incised and foul-smelling pus escaped.

Examination showed left chest less prominent, respiratory movement less, tympany below 5th rib. All the sinuses were healed save one below the spine of scapula which discharged blood, no pus or granules being evident. It admitted a probe to a depth of 11 cm.

February 9 patient failed to react to tuberculin. The sinus showed a tendency to close, with damming back of the discharge, accompanied by fever, headache and malaise.

On February 18 Dr. Follis opened the left side of thorax, removing a large portion of three ribs, all diseased. Through this opening, equal to the diameter of the underlying cavity, the whole space was carefully curetted, much pus and

necrotic tissue were removed, and the cavity was swabbed with carbolic, and irrigated with salt. Aside from a febrile attack, yielding to quinine, improvement was uninterrupted, the wound healing rapidly. After three weeks discharge was slight and granules had disappeared. KI was continued throughout, up to 40 gr. t. i. d. A sinus has persisted in spite of swabbing with carbolic several times. It admits a probe a few centimeters. Otherwise the wound has healed.

*Case. No. 3.*—F. S. G., male, white, 31 years old, fireman, from Sparrows Point, Md. He entered the hospital April 25, 1899, complaining of swelling over right side of stomach.

Except for attack of typhoid fever 4 years previous, his history was unimportant.

In September, 1898, he had a severe attack of colic, lasting three days, without chills or fever. In March following he noticed tenderness in the right lower abdomen, and soon after swelling, accompanied by some pain, especially at the end of the day. No gastro-intestinal symptoms. Examination showed a tumor in the right inguinal region, parallel to Poupart's ligament, 10 x 7 cm. It was firm, smooth, reddened in center and somewhat tender, and apparently in the abdominal wall. Left inguinal glands were shot-like, and the right larger and soft near the swelling.

On April 28 Dr. Finney incised the tumor, and opened into a superficial abscess in the abdominal wall. Considerable pus was evacuated and in the numerous yellow granules which it contained, the ray fungus was demonstrated microscopically. The abscess was curetted and drained with iodoform gauze. The patient's temperature was very irregular until May 4, reaching 106.6°; the leucocytes, 12,000.

On May 20, the wound had almost entirely healed from the bottom, the patient's condition was excellent, and he was discharged.

On October 20, 1899, he re-entered the hospital. After his discharge he had gone to Philadelphia, but in a few days had grown rapidly worse, and since then had been under treatment at different hospitals in that city.

He had lost much in weight and strength, and could not stand erect without pain. He limped on walking and inclined body toward affected side. A sinus persisted in the old wound, discharging thick, yellow, offensive pus.

On November 3 Dr. Finney again operated, excising the old granulating wound. A cavity was exposed from which three sinuses led. The first passed beneath Poupart's ligament, opening into a large cavity in the hollow of the ileum, which was roughened and eroded. The second burrowed deep under the femoral vessels; while the third extended to the cæcum and entered its lumen. All these were lined with granulation tissue and stringy yellow necrotic tissue, while sulphur granules were present in great numbers. The muscular abdominal walls were much weakened and showed fibrous changes.

The sinuses were all curetted out, the perforation of the

cæcum closed, the adjacent lymph glands removed, and the wound was packed with iodoform gauze.

The after-treatment consisted of irrigations of potassium iodide, 20 and later 40 parts to the 1000, until March, when bichloride, 1-50,000 was substituted. The sinuses were packed with bismuth gauze. Daily dressings until April; then every other day. Granules plentiful in discharge until March and never entirely absent. Internally KI was administered in increasing doses to 100 grains t. i. d., which was continued 4 months. The patient's condition improved. On April 26, 1900, the inner sinus measured 8 cm. in depth, the outer 18 cm. and they communicated. Rubber catheters were employed as drains; considerable discharge. Patient had been up and about the ward for a month and suffered no pain. On this date he was discharged at his own request.

On May 30, 1900, he was again admitted. Ten days before a lump had appeared above the great trochanter of the right femur, and was associated with a dull aching pain. The tumor now measured 5.5 cm. in diameter, was freely movable and slightly tender. From the old sinuses was a profuse discharge containing granules.

On June 2 Dr. Cushing incised this tumor and opened into a cavity communicating with the intra-iliac cavity via the middle portion of the iliac crest. A button of ileum was removed to make communication more direct. The old sinuses and the cavities were curetted out, swabbed with carbolic, and packed and drained with iodoform gauze. The treatment used on previous occasion was resumed.

About this time a lump appeared in right back, near the lumbar vertebrae. This grew to 4 cm. in diameter and was red, tender, and fluctuating.

On July 21 Dr. Mitchell incised this, evacuated several ounces of pus and many granules, and found a communication with old sinus over iliac crest. Cavity and sinus were irrigated and curetted.

On September 4 patient was discharged, two sinuses remaining, one from above iliac crest behind, to middle of Poupart's ligament, open at both ends, the other in back, 7.5 cm. deep. Slight discharge, no granules.

On May 20, 1901, patient reported. Had worked in Washington as fireman since discharge. Health excellent, weight increased from 148 to 170 pounds. Two small sinuses, one anterior, one posterior, persisted; slight discharge; no granules.

*Case No. 4.*—L. R., female, age 43, from Martinsburg, W. Va., white, manager of telephone office, unmarried. Entered hospital November 18, 1901, complaining of pain in right side. Family and personal history were negative.

In July, 1901, on three successive nights, she had been seized with sudden severe pain in right side, not radiating, becoming dull and heavy. This was followed by an illness confining her to bed three weeks, and at home three months. This was characterized by swelling over region of stomach, at times pain in right side radiating to groin and right breast,

while the right leg became almost paralyzed. There was no diarrhoea or blood in stools. Right side remained sore.

Four weeks preceding admission there was an exacerbation of the symptoms increasing in severity. Her appetite is poor, bowels irregular; she has lost weight, and has slight fever. Walking erect is painful. Sometimes she has trouble in voiding urine. One menstruation since March. No jaundice, sweats or chills.

General examination was negative. The abdomen was found full below umbilicus, depressed above, the abdominal respiratory movements very slight. The abdomen was tympanitic except in right flank, which was not so full as left, and was very tender on deep palpation, especially under ribs. The abdominal muscles were held firmly, without spasm, and on right side were almost board-like.

November 20, leucocytes 24,400.

November 22, leucocytes 36,200.

On November 22 Dr. Halsted explored the region about the liver and the right kidney. An area of necrotic tissue was found about tip of liver, from which *B. coli communis* was cultivated. Pain ceased after the operation. In the first dressing some suspicious granules were found. Wound was partly closed and drained.

On December 4 temperature rose to 101.7°, abdomen became full and tender 8-10 cm. beyond edge of sinus in old wound, and the discharge increased. No chill.

On December 19 Dr. Halsted carefully explored the right kidney, stripping off the fatty capsule. Kidney was small, hard, and flat. About the tip of liver pus was again found, its origin not determined. Considerable discharge followed at first and by February 10 only a small sinus remained in upper part of wound, admitting probe  $5\frac{1}{2}$  cm.

At this time pain developed in hypocostal region and on February 20 a new sinus appeared above the first, containing "sulphur" granules, in which the ray fungus was demonstrated. The patient did not react to tuberculin. She also did not tolerate KI, the administration of which was abandoned after one week. Discharge continued to be profuse and many granules therein.

On May 16 Dr. Halsted again operated, entering first abdominally, and then through the lower thoracic wall opposite some hepato-diaphragmatic adhesions, removing portions of two ribs. Between the diaphragm and liver was found a pocket of necrotic material connecting with the sinus in the right flank. This was curetted and drained. Improvement has been positive but very slow.

*Case No. 5.*—R. W. M., male, aged 43, from Lance, Stafford County, Va., white, occupation farmer, unmarried. He entered the hospital April 11, 1901, complaining of pain in right side.

His family and personal history were unimportant. In October, 1900, he suffered from attack of cramps in right side without accompanying symptoms, lasting two days. Pain was extreme and required morphia.

March 4, 1901, he caught heavy cold at Washington. Cough disappeared a few days later but pain in side returned and persisted. This pain was sharp and sticking, localized just above and to right of umbilicus, more severe at night and on lying down. Of increasing severity week preceding admission. No fever, chills, jaundice or diarrhoea. Had lost 20 pounds since onset, and on April 27 weighed 129½. On examination right costal margin found much more prominent than left, though respiratory excursion on two sides was equal and the lungs were negative. On palpation there was found a mass extending downward 13 cm. and with a sharply marked edge 3 cm. below costal margin. The individual costal cartilages were not palpable, overlying skin was oedematous and infiltrated. Mass extended beyond median line, was very tender and there was marked rigidity of muscles of right epigastrium. On percussion it was flat, merging above into liver dulness.

After admission temperature was irregular, never above 100.5° and reaching normal only seven days after operation. The urine contained occasional casts and a trace of albumin at first, then became normal.

A blood examination on April 20 showed: R. B. C. 3,800,000, hæm. 70 per cent, and leuc. 10,000.

On May 7, the day of operation, the leucocytes had risen to 21,000. During this time the tumor had increased considerably in size.

On May 7, under ether, Dr. Mitchell entered the abdominal cavity in the right upper quadrant. An abscess cavity was opened into, which contained thin yellow pus, full of typical yellow granules, in which the ray fungus was demonstrated microscopically, and from which there was a slight growth of colonies of actinomycosis in five weeks. The wall of the cavity was formed of necrotic omentum and liver, large masses of the latter being curetted out without reaching normal liver tissue. Iodoform gauze was used to pack wound. One month later patient was about ward. Discharge was very slight and no granules found.

On June 14, 53 days after admission patient was discharged at his own request. His weight was but 110½, but his condition was very good. Wound was apparently healing well and from base, and no granules were present. Shortly after returning home condition grew worse, the wound broke down, he suffered much pain in the abdominal region, rapidly lost weight and strength, and died August 22. There was no autopsy.

*Case No. 6.* (I am indebted to Dr. J. M. T. Finney for the following notes.)—C. H. G., a male, white, 46 years old, farmer, from Nut Bush, Warren County, North Carolina. He entered the Union Protestant Infirmary of Baltimore with symptoms of appendicitis. His past history was unimportant; there was nothing to lead to suspicion of infection with actinomycosis; he had had very little to do with cattle.

The attack resembled appendicitis with abscess formation and with that diagnosis he was brought to Baltimore for

treatment. At the operation, which was performed by Dr. Finney, an incision was made in the abdominal wall in the upper right inguinal region, and a large pus cavity was opened into. The pus was evacuated, the cavity packed and drained, and the patient subsequently left the hospital much improved.

He returned some time later with a recurrence of the symptoms and signs of an abscess cavity in the right renal region.

On April 17, 1900, Dr. Finney again operated, entering by an incision parallel to and below the costal margin. As in the previous instance a large abscess cavity was opened into, which had dissected its way along the outside of the ribs and into the flank, posterior to the mid-axillary line. Beyond this its course was not followed.

The contents consisted of a thin pus containing innumerable miliary granules of a yellowish color.

Because of its extent, complete excision of the abscess wall was impossible, but a considerable amount of infected tissue was removed, and the rest curetted. The cavity was then irrigated with bichloride of mercury, 1-1000, and packed and drained with iodoform gauze.

Microscopic examination of the infected tissue and the pus disclosed the presence of the ray fungus.

Potassium iodide in small doses was administered internally. The patient throughout had a temperature of from 99-101°, the wound healing but slowly, and on May 26 he again left the hospital improved. He returned home, where the disease later recurred and terminated fatally. No autopsy was obtained.

A study of these cases and of the 94 others reported by various American observers, makes possible several conclusions as to the nature of the disease, and suggests several lines of treatment, each having its more or less numerous supporters.

*I. Distribution.*—The cases are scattered widely throughout the country, although very naturally most of them are reported from the large medical centers. The residence of the patient is given in 96 cases. New York State furnishes 22; Illinois, 15; Massachusetts, 14; Iowa, 8; Maryland, 7; Pennsylvania, 5; Wisconsin, 4; California, Ohio, and Virginia, 3 each; Tennessee, Minnesota, and Alabama, 2 each; Colorado, Kansas, Kentucky, West Virginia, North Carolina, and Prince Edward's Island, 1 each.

It will be noted that less than 20 per cent of these come from southern states, which may account for the small number occurring in negroes, but three such cases being reported.

*II. Sex.*—72 were males, 23 females, while in 5 instances the sex was not mentioned. Leith, basing his results on 405 cases, gives 73 per cent males and 27 per cent females.

*III. Age.*—The youngest case reported was a child of 6 years, the oldest a man of 70. The disease occurs most frequently in middle life, as will be seen on arranging the cases according to decades—1-9 years, 1 case; 10-19, 9; 20-29, 16; 30-39, 19; 40-49, 12; 50-59, 9; 60-69, 6; 70, 1; age

not stated, 26 cases. Thus in 47 of the 72 cases in which the age was stated, 64 per cent, the patients were from 20 to 49 years of age.

*IV. Occupation.*—This is mentioned in 66 instances. There was a wide range, but those occupations appearing most frequently were farmers, 13 cases; cattlemen, 5; school children, 5; housewives (2 of these lived on farms), 4; stablemen, 3; carpenters (one had associated much with animals), 3; merchants, 3; clerks, 3; laborers, 3; and physicians, 2. Thus in 24 cases, 36 per cent, the patients had had much to do with both livestock and grain.

*V. Duration.*—In one instance the disease continued but four weeks; in another, 13 years. In 14 the duration was 3 months or less; in 11, 3-6 months; in 18, 6 months to 1 year; in 15, 1-2 years; in 12, over 2 years; while in 28 cases this was not given.

The chronic character of the disease is well shown by the fact that in 44 cases, 62 per cent, it lasted over 6 months, and in 27, 37 per cent, over 1 year, though all the cases were under treatment to a greater or less extent.

*VI. Infection.*—Usually there is no definite history of infection. The disease, as occurring in man, is probably in a large majority of cases contracted from animals, especially cattle, in which actinomycosis, usually known under the name of "lumpy jaw" or "big jaw," is not uncommon; or in common with cattle, from grain.

In six of the cases there was a definite history of caring for an animal suffering from "lumpy jaw" during a considerable period preceding the manifestation of the disease in the patient.

In several cases, too, there was a history of habitually chewing grain or straws. The fact that the streptothrix actinomycotic habitually gains entrance to the human body by way of the mouth or the nose, sufficiently accounts for the large proportion of cervico-facial cases, 53 per cent, reported in this series.

In 18 of these cases (cervico-facial) the entrance of the organism could be located definitely in a carious tooth, a fragment of grain being found imbedded in the cavity in one instance; while in 3 others entrance was gained through a wound, caused in the different cases by a clamp for artificial teeth, a tooth-pick broken off beneath the tongue and not removed, and an oat straw in the same location. In still another instance the nucleus of an actinomycotic abscess in the submaxillary region was found to be the fragments of a beetle.

Of the 4 skin cases, there was an external wound in 2, while in a third the patient was accustomed to sleep in the stable straw, with his back and shoulders, the seat of the lesion, unprotected.

*VII. Clinical Characteristics.*—These vary greatly with the region of the body involved. In the cervico-facial and cutaneous, as well as in many of the thoracic and abdominal cases, which first show themselves in the subcutaneous tissue of the walls of these cavities, the first symptoms noticed are

pain and swelling. This pain is not often severe, and may be entirely absent.

The swelling gradually increases in size, the tissues become red, firm, and develop a board-like resistance, while outside this area is a zone of marked oedema. The center of the involved area after a longer or shorter interval becomes fluctuating, and there follows a spontaneous discharge of the contents of the actinomycotic abscess cavity. The contents are a thin, clear, syrupy fluid, containing occasional or innumerable bodies varying in size from a pin point to a large pin head, of a pearly-gray to yellowish-white color—the so-called "sulphur" granules.

The abscess contents having thus, by the formation of a sinus, succeeded in escaping from the cavity, whose walls of densely infiltrated connective tissue tended to form a constantly increasing barrier to the spread of the disease in other directions, continue to discharge.

At this stage infection by pyogenic organisms is prone to occur, and the discharge becomes purulent in its character. The sinus too usually becomes choked by an exuberant growth of granulation tissue, pus reaccumulates in the site of the old cavity, and presently escapes in its turn from some newly formed sinus, the process repeating itself indefinitely.

In actinomycotic cases high fever is not marked, the temperature of the patient usually running more or less irregularly between normal and 101° F.

Examination of the blood shows a leucocytosis, varying in the 7 cases reported (4 in this hospital) from 8000 to 36,200, and averaging 17,000.

Three cases in the Johns Hopkins Hospital, in which an injection of tuberculin was administered for diagnostic purposes, failed to give the febrile reaction characteristic of tuberculosis.

The cervico-facial cases are often mistaken at first for ordinary toothache, and teeth are thereupon extracted without relief. Trismus is a marked symptom, often being so severe as to necessitate a liquid diet. These cases, if uncomplicated, are unaccompanied by marked general symptoms.

In the thoracic forms the first symptoms are those of a bronchitis or pleurisy, the disease in 9 of the 20 thoracic cases seeming to confine itself chiefly to the pleural cavity and thoracic wall.

Later on the symptoms become more severe, especially in the bronchial cases, often presenting a picture typical of phthisis—irregular fever, sweats, chills, cough, purulent or blood-stained sputum, loss of strength and emaciation. Profuse hemorrhage from the lungs is, however, rare, only one case being reported, and the sputum is only occasionally blood-tinged. Contrary to the usual rule in tuberculosis of the lungs, the bases were involved primarily in 7 cases, the apices in but 3, of the 10 cases in which the location of the lesion was reported. On careful search the ray fungus can be found in the sputum.

The abdominal cases often resemble appendicitis, and the

appendix and the cæcum are the parts of the intestinal tract most frequently involved primarily. In five cases they were definitely mentioned as being involved, and such was presumably the fact in several others.

The liver is also frequently affected, but apparently always secondarily to a lesion of the intestinal canal (5 cases) or the lungs (2 cases).

*VIII. Diagnosis.*—Notwithstanding the fact that many of the symptoms of actinomycosis are very characteristic of that disease, diagnosis should never be positive without the finding of the organism—the ray fungus.

This occurs in the sulphur granules of the abscess contents, or much less frequently in the walls of the cavity. In man all three characteristic elements are found, but the long branching threads and the coccus-like bodies are more often seen than the bulbous processes, and are sufficient for establishing a diagnosis.

The presence of bodies in the discharge resembling sulphur granules, observed macroscopically, is not sufficient for a diagnosis, as under the microscope these are frequently found to be clumps of bacteria, tuberculous debris, etc. The cultivation of the organism, which is an anaërobe, is attended with difficulty and growth is slow.

In the American cases the "sulphur" granules were almost invariably found, while the ray fungus was definitely stated to have been observed in 71 of the cases.

*IX. Location.*—As far as could be determined from the histories, the primary lesion occurred in the region of the cheek or upper jaw in 11 cases, in the lower jaw or neck in 42 cases, a total of 53 in the cervico-facial region; in 20 instances in the thoracic region, in 23 in the abdominal, while in 4 the disease appeared to be primary in the skin.

Illich (as quoted by Ruhräh), in a collection of 421 cases, gives the primary involvement as follows: of head and neck 55 per cent, pulmonary 15 per cent, abdominal 20 per cent, cutaneous 2.5 per cent, unknown 6 per cent.

*X. Extension.*—Although the progress of the disease is sluggish, extension is prone to follow, either by direct involvement of contiguous tissues, or by metastases, the blood current acting as the carrier.

The first is by far the most common, and is well illustrated by several cases.

Thus in the case reported by Fütterer the primary lesion was found at autopsy in the lower lobe of the right lung, the diaphragm and liver being involved in succession.

In Bullitt's pulmonary case the disease was found at autopsy to have extended along the sheaths of the psoas muscles, reaching the iliac fossa on one side.

In Keen's case (Ruhräh's Summary, No. 65) the disease, spreading from the subcutaneous tissue of the arm, eroded the axillary artery, an almost fatal hemorrhage resulting, while in Hudson and Flexner's case (Ruhräh, No. 59) the disease, which had commenced as a "running sore" over the right scapula, was found at autopsy to have involved both lungs.

In the pulmonary cases the pleuræ are involved sooner or later, the actinomycotic abscess tending to discharge on the surface by means of a sinus.

In 17 of the 20 thoracic cases the abscess contents reached the thoracic wall and discharged either spontaneously or through an incision. The ribs or vertebræ were involved secondarily in 9 of the thoracic cases, the ileum in one abdominal case, while in 11 of the cervico-facial cases there was bone involvement.

That the disease may reach other portions of the body by the blood current is also definitely proved.

Fütterer's case, above mentioned, furnishes a beautiful example of this, two actinomycotic nodules being found at autopsy at the base of the tricuspid heart valve.

There is no proof of extension of the disease by way of the lymphatic system and it probably does not occur, enlargement of the lymphatic glands, or other evidence of infection by that channel, being conspicuous by its absence.

**XI. Prognosis.**—Recovery occurred in 45 cases, improvement in 14; in 9 no improvement was noted or the case was lost sight of, while in 32 there was a fatal termination.

Ruhräh, reporting on the first 58 cases, gives the following percentages: Recovery, 29.29 per cent; improvement, 7.44 per cent; no improvement or case lost sight of, 17.42 per cent; and death, 47.24 per cent.

The prognosis depends largely on the location of the disease, the pulmonary cases showing the highest mortality, the cervico-facial the lowest:

	Cervico-facial.	Abdominal.	Skin.	Pulmonary.
Recovery .....	36—67.9%	5—31.7%	2—50%	2—10%
Improvement .....	7—13.2	5—21.7	..	2—10
No improvement or lost sight of.....	5—9.4	3—13.0	..	1—5
Death .....	5—9.4	10—43.4	2—50	15 75
No. of cases .....	53	23	4	20

**XII. Treatment.**—43 cases were treated surgically, 23 by excision of the affected tissue, and 21 by simple free incision and curettage. Both methods were followed by irrigations, usually of bichloride of mercury in weak solutions, and by packing and drainage with iodoform gauze.

34 cases were treated surgically, 11 by excision, and 23 by incision and curettage, with after-treatment similar to the above, while iodide of potassium was definitely stated to have been used at the same time as an internal medicine.

In 9 cases potassium iodide was administered without surgical treatment.

In 1 of the 2 thoracic cases in which complete recovery occurred (Ruhräh, Case No. 33), oil of eucalyptus alone was used (both internally and as a spray). In one cervico-facial case and in one abdominal case, recovery followed injections of cinnamyl and muriate of cocaine, and zinc and silver nitrate respectively.

In 11 cases the treatment was not reported.

In a large proportion of the cases treated surgically, repeated operations were necessary before recovery occurred. The disease exhibited great stubbornness and recurred almost

invariably after simple incision and drainage, and not infrequently after what was believed to be complete excision of the affected tissue.

Good results have followed in the cases in this hospital only after the latter treatment, though in 3 of the cases in connection with less complete operations potassium iodide had been administered previously in large doses and for long periods.

Sawyers of Iowa strongly recommends in addition to the internal administration of potassium iodide, its injection hypodermically into the affected tissues. He reports three cases treated in this way without operation, two of which, one a pulmonary case in which the ray fungus was demonstrated in the sputum, were followed by recovery, while a third, at the time of his report, was practically well.

His treatment consists in the injection of from 15 to 30 minims of a 1 per cent aqueous solution of potassium iodide at intervals of from 3 to 4 days at first, but later more infrequently. In one case 41 injections were administered, while in the pulmonary case 25 injections were made through the thoracic wall directly into the lung tissue. The only unpleasant effects noted were increased swelling and sometimes pain for a period of about 12 hours following the injection.

The data regarding the 43 cases in which potassium iodide has been used internally in the treatment of actinomycosis are very incomplete. In 4 cases it was certainly discontinued without a fair trial, while in the remainder the duration of the treatment is only infrequently given. The amounts also varied greatly, ranging from 15 to 600 grains daily.

Lieblein, of Wölfler's clinic, Prague, in an article on the subject appearing in "Beiträge für klinische Chirurgie," Vol. XXVIII, p. 198, gives the results of potassium iodide treatment in connection with surgical incision in 62 cases, in 49 of which the disease was located in the cervico-facial region. On comparing these with the 21 American cervico-facial cases in which potassium iodide is mentioned as part of the treatment, and the 32 in which no mention of it is made, it will be seen that his results are very similar to those of the latter class of American cases. Both are more satisfactory than the results of those American cases treated with the drug, which in 4 instances was not associated with any surgical procedures. Cervico-facial cases:

	No.	Recovered Cases.	Improved Cases.	Non-improved, includes 1/2 cases still under treatment.	Died—Cases.
1. Lieblein .....	49	36—73%	6—12%	4—8%	3—6%
Amer- { 2. K. I. treat. ....	21	12—57	5—24	1—5	3—14
ican { 3. No K. I. treat. ....	32	24—75	2—6	4—13	2—6
4. (2 and 3 combined) .....	53	36—67.9	7—13.2	5—9.4	5—9.4

The drug probably has no specific action on the ray fungus, as this has been found in the body tissues after months of systematic potassium iodide treatment.

Its use is generally recommended in connection with free incision and drainage of the actinomycotic abscesses as they

appear, when the best results are seen. The action of the potassium iodide, as stated by Lieblein, is to bring about a solution of the cellular infiltration about the abscess cavity, and the consequent discharge of the ray fungus, in imitation of nature's own method of healing.

Porter of Boston, in his report of 8 cases occurring in his own service, grants that the drug "has distinctly influenced some cases for good and should be used in connection with the local [surgical] treatment." He advises, notwithstanding, the complete excision of the affected tissues wherever possible, a conclusion much in accordance with that drawn from results obtained here.

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## REPORT OF TWO TESTICULAR TERATOMATA WITH A REVIEW OF THE RECENT LITERATURE.

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The problems which are to be solved in regard to the origin, development and structure of teratomata in general, and especially of those occurring in the ovary and testicle, have aroused a widespread interest among pathologists, as is shown by the rapidly increasing literature on this subject.

A brief review of the recent literature, therefore, seems pertinent, and at the same time we wish to report two cases of teratoma of the testicle.

**CASE I. Clinical History.**—Patient 29 years old, married; occupation, porter.

Family history is negative.

**Past History.**—Has always enjoyed good health. No history of syphilis or other venereal disease.

**Present Illness.**—No history of trauma. Noticed a painless enlargement of the left testis, about six months previous to admission to the hospital, which increased in size, but was not accompanied by pain. Testis removed at operation on January 3, 1901. Recovery uninterrupted and patient was discharged in nine days. On April 13, 1902, the patient has just recovered from an attack of typhoid fever. There is no evidence of recurrence. No discoverable metastases.

**Pathological Report.**—The specimen consists of a globular tumor measuring  $10\frac{1}{2} \times 9 \times 7$  cm., which represents an enlarged testicle. The epididymis and the vas deferens appear normal. The veins of the pampiniform plexus are slightly enlarged. The outer layer of the tunica vaginalis is somewhat thickened; its inner surface smooth. The visceral layer is also smooth, and contains numerous dilated veins. On section the testicular

parenchyma is entirely displaced by a soft bulging new growth. The appearance of this varies in different parts. It seems to be made up for the most part of a series of small cysts, varying from 1-3 mm. in diameter, which are closely set together, and which are separated into groups by bands of connective tissue. In some places the amount of connective tissue is quite large. The tumor shows yellowish areas of necrosis and occasional areas of hemorrhage. The fluid which is contained in the cysts is clear and slightly mucilaginous. Besides the cysts there are small translucent grayish areas in the stroma, which have the appearance of hyaline cartilage.

**Microscopic Examination.**—At the margin of the tumor a few tubules of the testis are found, which appear normal. Immediately within these is a connective tissue capsule containing a few dilated capillaries.

For convenience the descriptions of the cysts and stroma are given separately.

**The Cysts.**—Are found scattered generally throughout the tumor, and in most instances have an epithelial lining, although this is occasionally absent. In outline they are very irregular, due in part to the uneven growth of the epithelial lining, in part to the character of the connective-tissue wall. The contents of the larger cysts have escaped, but in the smaller ones consist of albuminous material, degenerated epithelial cells, and in some instances polymorphonuclears. The epithelium lining the cysts varies from the flat squamous to the columnar type and may be of simple or stratified variety. The flat epithelium is confined mostly to the larger cysts where the cells seem drawn apart. Generally in single layer, they are stratified at rare intervals. The individual cells show a vacuo-

lated protoplasm containing a nucleus with indistinct chromatin network. Certain cysts contain epithelium which has undergone keratohyaline change, forming epithelial pearls, and leaving only a single layer of epithelial cells as a lining. Solid nests of epithelial cells are present, smaller than the above cysts. The peripheral cells are columnar and closely packed together, those toward the center become flattened, and finally undergo keratohyaline change. By the osmic acid method of Kolossoff intercellular bridges can be distinctly demonstrated in these solid epithelial nests. Cysts containing both squamous and columnar epithelium can be found, and no definite line of demarcation between the two varieties of epithelium is apparent; the transition seems gradual. Pure columnar epithelium lining the cysts is rarely seen, nevertheless it is present. The variety is always simple or pseudo-stratified, and the peripheral protoplasm contains zymogen granules. No ciliated epithelium or goblet cells could be demonstrated. Irregular and tortuous clefts in the stroma lined by cuboidal or squamous epithelium occur here and there in the sections and resemble the cysts above described, with the exception of the very irregular outline. Small alveoli lined by simple columnar epithelium are present, and round about them the epithelial tissue has the appearance of having undergone carcinomatous change. The cells are closely packed together into irregular nests and seem to be invading the surrounding stroma in every direction. The nuclei in these areas are large, oval or round with distinct chromatin network and often appear vacuolated. The protoplasm is mostly degenerated, and the cell outline indistinct. A transition from the gland alveoli to these malignant epithelial nests is apparent in some places.

*Stroma.*—Connective tissue forms the predominant element and presents a variety of types. The most frequent is the ordinary white fibrous tissue with wavy fibres and elongated irregular nuclei. Where the tissue is very dense and the nuclei very closely arranged, it bears a striking resemblance to sarcomatous tissue. Myxomatous tissue with very loosely arranged fibres, and large nuclei with distinct nucleoli, is present, but in small amounts. Smooth muscle arranged in bundles running in all directions is found in all portions of the tumor. About the larger cysts the muscle forms a circular layer, but definite outer longitudinal and inner circular layers are not found. Cartilage exists in the form of small islands with circular outline, which are surrounded by connective tissue from which the cartilage appears to be developing. Only the hyaline variety is present. Adipose tissue is present in small amount. Lymphatic tissue occurs especially about the epithelial elements and cysts, but no definite corpuscles of Malpighii are found. The blood supply is poor. No well defined vessels are found, but here and there are spaces in the connective tissue containing blood corpuscles and resembling dilated capillaries. No elastic tissue could be demonstrated by Weigert's method.

In this tumor we have tissues derived from all three germinal layers. From the ectoderm the squamous epithelial nests with peripheral columnar shaped cells, which gradually flatten toward the center finally to undergo keratohyaline degeneration, and the cysts with squamous epithelial lining. The former represent the epidermis.

From the ectoderm, the gland alveoli with columnar epithelial lining and epithelial nests, which have the appearance of having undergone malignant change.

Microscopically it has every appearance of malignancy, and this fact, together with its general distribution throughout the tumor, lead us to believe, in spite of the fact that the subsequent history reveals no recurrent growth, that this represents a true carcinoma. The mesoderm is represented by the connective tissue, smooth muscle and the islands of cartilage. The

tubules of the testis are normal; also the epididymis, vas deferens and veins, so that this malignant growth must spring from the elements of the tumor. Some cysts containing two types of epithelium were described. Gessner<sup>1</sup> explains these by a junction of two cysts, each having a different epithelial lining.

#### CASE II. No clinical history can be obtained.

*Pathological Report.*—The tumor consists of a mass with the general shape of the testicle measuring 9 x 7 x 7 cm. Its outer surface is smooth and covered by a double membrane, which represents the tunica vaginalis. The outer layer of the tunica is smooth and normal in appearance, both externally and internally. It contains a number of rather large veins. The inner layer of the tunica vaginalis forms the capsule of the tumor. It is slightly and uniformly thickened. Numerous large blood channels can be seen coursing through it. In places it is attached firmly to the tumor, in other places only loosely. The tumor differs in consistency in different parts; in some places it is solid, in others cystic. The epididymis is not apparent to the eye. On section the cut surface of the tumor is very irregular, contains circumscribed portions bulging above the general level and other depressed areas, which seemingly represent small cyst cavities. The elevated portions also seem to be thin walled cysts, containing a clear fluid, either watery or mucilaginous. Between the cysts, which vary in diameter from one to nine or ten millimeters, the tissue is of a homogeneous gray-white color. In this tissue a number of small cavities are present, some of which seem to be blood vessels, whilst others are perhaps small cysts. The portion of the tumor representing in position the epididymis presents a different appearance. It is apparently firmer than the rest of the tumor and of a mottled appearance, the predominating color being a reddish-brown, this appearance giving one the impression of being due to altered blood. The cord measures about 2 mm. in diameter, is uniform in size, not nodulated, and is pervious throughout. About one pole of the tumor there seems to be an area of normal testicular tissue. Microscopic examination of the fluid from the cysts shows epithelial cells which have undergone fatty degeneration, red blood corpuscles and small refractive bodies, which look like the heads of spermatozoa.

*Microscopic Examination.*—From the naked eye appearances and a comprehensive study of the sections we can divide the tumor into three parts, cysts, stroma, and the hemorrhagic portion corresponding in position to the margin of the tumor. The cysts as noted in the gross description vary greatly in size, and are simple in formation. The cyst contents have escaped. Epithelium showing wide variation in structure forms the cyst lining. The lining in the majority of the cysts is of the columnar type, and of the simple or pseudo-stratified variety. Cilia are noted in some instances. Goblet cells clothe the cysts in other instances, and here shallow infoldings are noted resembling simple tubular glands (anlage of the digestive tract). Offshoots from the cysts in the form of fine processes with epithelial lining suggest strongly that in some instances they communicate one with another. Squamous epithelium is not at all frequent. It was only once noted, but here was of typical appearance, and occurred in the form of a cellular island, the center of which contained an epithelial pearl. In only one place does the epithelium appear to have taken on malignant characteristics. This area is near the margin of the tumor, since alveoli testis border it, and is in the form of a nodule separated into compartments by trabeculae of connective tissue. In these compartments are cells of peculiar

<sup>1</sup> Gessner, Deutsche Zeitschrift für Chirurgie, 1901, ix, 86-126.

appearance with cell outline indistinct, and protoplasm degenerated. The nuclei are very irregular in size and shape, in some cases almost completely filling the cell, in others small and crescent-shaped. At times the nuclei appear to exist alone without protoplasm. The arrangement of the cells is quite indefinite, except in a few places where true gland alveoli provided with columnar epithelium exist. A gradual transition from the normal appearing alveoli to the irregular cells above can be traced without difficulty. No mitotic figures were present. The stroma of this nodule is composed of fibrous connective tissue in which are found many lymphocytes and plasma cells. At one point on the margin of the tumor just inside the capsule we find a very peculiar tissue. What the distribution of this tissue is cannot be determined since it was not noted in the macroscopic description, but in all sections cut at the margin of the tumor it is constantly present. The arrangement of the tissue is in columns, which have apparently a tortuous course and enclose within their spaces masses of blood clot. The columns are very irregular in outline and vary in thickness, at times being only the width of one cell. The manner of growth is distinctly malignant in appearance, for it seems to be invading blood vessels in the neighborhood, pushing in the endothelium before it. It also is growing into the blood clot. It is attached to the compact connective tissue which is at the margin of the tumor, and extends along trabeculae which run toward the center of the neoplasm. It also exists without supporting tissue as irregularly circular masses or finger-like processes. A study of the individual cells shows that we have two varieties to deal with. For a comparison of these we have taken an area where the tissue exists by itself without supporting stroma. The most noticeable thing is the fact that there is no stroma, the cells being closely packed together without apparent support. The smaller of the two varieties of cells have a fairly definite outline and are of an oval, circular, or quadrilateral shape. They are about the size of decidual cells. The protoplasm takes eosin well and is slightly granular. It shows a tendency to degenerate, being absent in some cells. The nuclei are oval or circular, fairly small in proportion to the size of the cell, and stain almost solidly so that no chromatin network can be seen. A few mitotic figures were noted in these cells. The larger cells are many times the size of the ones just described, and much more irregular in shape. They appear as mere masses of protoplasm in which are nuclei, no cell division being apparent. These protoplasmic masses are sometimes in long and very narrow strands. The protoplasm is quite granular and stains very deeply in eosin. In places it has degenerated, giving an areolar appearance to the tissue. The nuclei are large and very irregular in shape and size. They show a distinct chromatin network with one or two distinct nucleoli. Small oval masses of protoplasm containing many nuclei resemble giant cells. Occasionally single cells exist. Mitotic figures are numerous. Among these cells are found red blood corpuscles, but no blood vessels or stroma of any kind. The blood clots which this peculiar tissue surrounds present no unusual features, except that they contain more leucocytes than usual.

*Stroma.*—White fibrous connective tissue forms the basis and is arranged in the form of bundles running in and out between the cysts. In some areas it is compact, in others, definitely myxomatous. Smooth muscle is present in large amount, disposed in bundles running in all directions. In some areas the muscle forms a circular and longitudinal coat about the cysts. No cartilage, elastic tissue or bone is present. The epididymis has been the seat of hemorrhage but is otherwise unchanged the tubules appearing normal.

As derivatives of the entoderm we have in this tumor the cysts and spaces lined by columnar epithelium often ciliated and often containing goblet cells. The mesoderm is represented by the connective tissue and smooth muscle, which is often arranged in layers about the cysts. Cysts with infoldings of the lining epithelium, with submucosa, and surrounding layers of smooth muscle represent an anlage of the intestinal tract. The ectoderm has not developed to any extent as only one nodule was found containing squamous epithelium with a central epithelial pearl. The peculiar tissue at the margin of the tumor is confusing. The larger cells have all the characteristics of syncytial cells, and we believe this to be their true interpretation. The smaller cells are hard to explain; they seem quite distinct from the larger cells although placed in among them. They do not appear to be an early stage of syncytium, but have rather the appearance either of decidual cells or cells of Langerhans' layer. The arrangement of the syncytium-like cells into long strands, and their marked tendency to invade the surrounding blood vessels and blood clot, strongly suggest a malignant character. A comparison with sections from a true deciduoma malignum showed a striking resemblance between the two.

It must be remembered, however, that this tissue is confined to the margin of the tumor, that the epididymis, vas deferens and veins of the pampiniform plexus are normal, that it is necessarily developing within narrow confines which possibly tends to the development of invasive characters. Taking into consideration these facts, and with no clinical evidence of metastases, we feel that we cannot say positively that we are dealing with a malignant growth of syncytium, although this is the most plausible interpretation.

Since the appearance of Wilms' <sup>2</sup> articles, numerous teratomata of the testis have been reported, and from the literature we have collected twenty-four cases. A brief history of these cases is given.

**CASE III. Wilms.**—Patient 50 years old. History of injury to testicle 15 years previous, from which patient dates the beginning of the tumor. The tumor is entirely within the tunica albuginea. The spermatic cord and vas deferens are normal. On section numerous cysts are present, and small islands of cartilage are noted. Some of the cysts communicate one with another by means of canals.

Under the microscope the tumor tissue is seen to be composed of elements of all three germinal layers. The ectoderm is represented by cysts lined by squamous epithelium in which were also epithelial pearls. The mesoderm is represented by connective tissue, frequently of embryonic type cartilage, bone, smooth and striated muscle and lymphatic tissue. The entoderm by cysts lined by high cylindrical epithelium, which show glandular depressions in the form of offshoots from the main cyst which are lined by cuboidal epithelium. The close relationship between these cysts and the cartilage suggests a tracheal anlage. At the margin of the tumor is found a capsule of connective tissue, and beyond this again degenerated testicular canals.

**CASE IV. Clinical history not given.**

Tumor measures 13 x 8 cm., and is enveloped by tunica albuginea. The tumor can be divided into three parts, a central cystic portion, and a solid portion at each pole. The cystic

<sup>2</sup> Wilms, Beiträge zur Pathologischen Anatomie u. zur Allgemeinen Pathologie, 1896, xix, 233-366.

Deutsche Zeitschrift für Chirurgie, 1898, xlix, 1-25.



Teratoma of testicle, showing syncytial cells and cells of Langerhans' layer invading blood space.



portion is supported by trabeculae of connective tissue, in which are islands of cartilage. The cysts are connected one with another in some instances. The epididymis is normal.

On microscopic examination it is seen that the central cystic portion is constructed of tissue derived from the three primary germ layers. Cysts provided with columnar or cuboidal epithelium in simple or stratified variety, the individual cells showing now a granular protoplasm, now a distinctly mucous character, are very numerous, and are derived from the entoderm. The arrangement of such a cyst with submucosa and muscularis about it suggests an anlage of the digestive tract. Cysts provided with a lining of squamous epithelium, in the center of which epithelial pearls are often found, have their origin from the ectoderm. In the beginning of its growth the squamous epithelium is in the form of solid processes, and only later becomes cystic by degeneration of the central cells. The arrangement of the cells is the same as that found in the skin; the outermost cells corresponding to the stratum Malpighii gradually become flatter and keratinized finally to the epithelial pearl. These epithelial structures are surrounded by a stroma developed from mesoderm consisting of connective tissue of all varieties, cartilage and smooth muscle. Where the cell growth has been prolific the tissue resembles that found in sarcomata. The rapid growth of the whole tumor has led to considerable necrosis. Within the albuginea remains of testicular parenchyma are still to be made out.

CASE V. Diameter of tumor 10 cm. The cord and epididymis appear normal. The whole tumor is surrounded by the tunica albuginea and the tunica vaginalis. The main portion of the tumor is in the center of the testis, and at each pole there is one smaller nodule.

*Microscopic Examination.*—Degenerated testicular parenchyma is noted at the periphery of the tumor, especially at the poles. From the ectoderm are found canals and tubules, sometimes hollow and lined by squamous epithelium, sometimes solid with a central epithelial pearl. These structures are quite numerous in contradistinction to the cases above reported. From the entoderm the cysts lined by cylindrical epithelium are derived. The character of the epithelium is influenced much by the intracystic pressure, the cells being in some places flattened and separated. Many mucus-secreting cells are present, also a few gland alveoli. The occurrence of some cysts with a circular muscularis, lymph follicles, cartilage and glands is interpreted as an anlage of the respiratory tract. The stroma contains connective tissue of both mucous and white fibrous types, cartilage, and smooth muscle. The stroma is more abundant in the central tumor than in the polar nodules. In portions of the tumor the tissues bear a close resemblance to sarcoma and carcinoma. At the upper pole where the tissue appears sarcomatous the albuginea has been penetrated, and the epididymis involved. Whether this growth has originated from the interstitial tissue of the testicle or from the mesodermic elements of the teratoma cannot be determined.

CASE VI. Patient 27 years old.

The spermatic cord and epididymis are apparently normal. The albuginea and a variable amount of testicular parenchyma surround the tumor. A few small cysts are scattered throughout the tumor. In the stroma islands of cartilage often collected into groups are noted. The blood vessels appear especially numerous.

*Microscopic.*—The spaces lined by squamous epithelium in their early development are solid, a lumen later being formed by degeneration of the central cells. The strata Malpighii, granulosum, and corneum are distinct. In contrast to these

are the cysts lined by high columnar non-ciliated epithelium, with definite submucosa and circular muscularis, evidently an intestinal anlage. Numerous glandular structures open into the cysts, but there has not been sufficient differentiation to admit of comparison to any organ. A loose embryonic connective tissue forms most of the stroma, in which are found many islands of hyaline cartilage. Smooth muscle, generally arranged in a circular manner about the epithelial cysts and tubules, is abundant. The blood vessels, which as above noted are very numerous, have not reached any mature development, and are still embryonic. On the border of the tumor are found true testicular canals which have been much compressed by the growth of the tumor, and in some places simulate a definite capsule. Between the testicular canals the interstitial cells of Leydig have undergone proliferation. The growth of this tumor was very rapid, reaching the size of a child's head in ten months.

CASE VII. Tumor measures  $15 \times 7 \times 10$  cm. Vas deferens widened but otherwise normal. In the course of the pampiniform plexus nodules of tumor can be traced, which on section have a cystic structure. The epididymis is present, but its relation to the testicle is no longer clear. The tumor can be divided into three distinct nodules. The uppermost is hard and apparently free of cysts, but contains fine canals which look like blood vessels. The rete testis is not sharply separated from this nodule. The middle nodule shows cysts, canals and a stroma containing islands of cartilage. The lowermost nodule contains many cysts and canals, and is separated from the nodule above by a capsule.

*Microscopic.*—Only a small amount of testicular tissue remains and this is much degenerated. Tissues developed from all three germinal layers are present. Cylinders filled with squamous epithelial cells arranged in layers corresponding to those found in the epidermis. Cysts lined by cylindrical epithelium communicate one with another; glandular structures open into them. Mucous cells are abundant. Some of these cysts are in close relationship with smooth muscle and cartilage representing an anlage of the respiratory tract. Smooth muscle, cartilage, and several forms of connective tissue form the stroma. The nodules above described have the same elements, but the upper one is in an earlier stage of development. The nodules in the veins of the pampiniform plexus show a structure derived from the three germinal layers.

CASE VIII. No clinical history given.

Tumor measures  $12 \times 8 \times 8$  cm. Surface smooth and covered by tunica vaginalis and tunica albuginea. One vein of the cord is distended with a tumor nodule. The epididymis is somewhat compressed by the tumor, but its canals appear normal. The tumor is compact, and on section is composed of an aggregation of small nodules, some of which are solid, some cystic. In the cystic portions the interstitial tissue contains islands of hyaline cartilage.

*Microscopic.*—Canals of the testes are found only by study with the microscope, and are located here and there within the capsule. Their epithelial structures are much degenerated. In the more compact nodules the elements of the mesoderm preponderate, connective tissue, cartilage and smooth muscle. In the cystic portion the connective tissue is myxomatous in character. The cysts are lined by cylindrical epithelium, sometimes of single, sometimes of stratified variety, and contain many mucous secreting cells. Processes resembling gland alveoli open into the cysts in places, their functional characteristics, however, cannot be determined because of their early stage of development. The epithelium has grown into the con-

nective tissue in such a way as to suggest carcinoma. These cysts are in close relationship with the smooth muscle and cartilage as described in the above cases. Squamous epithelium possessing the characteristic arrangement of the epididymis is found in small amount lining cysts, or in the form of solid cylinders. The tumor nodule in the vein mentioned has not the characters of the teratoma, but is a round-celled sarcoma.

CASE IX. Patient aged 43. Noticed a tumor nodule in testis the size of a hazelnut, which in nine months attained the size 10 x 7 cm. The tumor has developed within the substance of the testicle as is proven by the covering of tunica albuginea, or where this has been removed in a previous examination by true testicular parenchyma. In places the tumor is fluctuating, and on section many spaces and cysts are found. The contents of the cysts are in some cases atheromatous, in others colloid-like. Pressure of growth has influenced the shape of the cysts, and the walls of some have been broken through. Communication between cysts is noticed in some instances. The stroma is small in amount, cartilage is rare, and the blood vessels not well developed.

*Microscopic.*—What remains of the testicle at the margin of the tumor is compressed to form a sort of capsule for the tumor. The large spaces are lined by mucous membrane containing many goblet cells. Among the detritus in the lumen some ciliated epithelial cells are found. In smaller spaces the ciliated epithelium lining is distinct. About many of the spaces and cysts the muscle is arranged in circular or longitudinal layers as in the intestine. No lymph follicles are found. The cysts often are beset with connective-tissue papillae, resembling the crypts in the intestine. Squamous epithelium lining cysts, or as solid nests, could not be found although its absence in the tumor cannot be affirmed since all the tissue was not examined. The stroma is composed as usual of connective tissue, smooth muscle and cartilage, but is not abundant because of the great number of cysts.

CASE X. Patient aged 29. Half a year after extirpation metastases developed in the region of the liver. Autopsy findings unknown.

Tumor measures 5 x 7 cm. The epididymis, plexus pampiniformis, and vas deferens normal. On the upper, posterior and lower surfaces normal testicular parenchyma is seen. The presence of testicular tissue on the posterior surface makes the development of the tumor from the rete testis out of the question. The tumor consists almost entirely of cysts, some of which are united by canals. The stroma is small in amount and contains a few islands of cartilage.

*Microscopic.*—The parenchyma of the testicle is normal although in some instances the canals are packed solid with epithelial cells. Cysts provided with a lining of high cylindrical epithelium are numerous, and from them glandular alveoli spring. These alveoli are lined by cubical epithelium with no mucous secreting cells. Some of the cysts contain ciliated epithelium. Beneath the lining epithelium a loose submucosa of connective tissue and a large amount of smooth muscle are present. The islands of cartilage are often surrounded by smooth muscle, and extend directly into the cysts in some cases, or by their growth push in the epithelium which may be the only structure between the cartilage and cyst cavity. This could explain the cases reported with cartilage in the testicular canals. The cysts with ciliated epithelium and surrounding smooth muscle, and the cartilage are interpreted as an anlage of the respiratory tract. The ectoderm is represented by cysts and spaces clothed with squamous epithelium.

A few epithelial pearls are found. From the mesoderm the connective tissue, often of embryonic type, the smooth muscle, and the cartilage are developed. The blood vessels are also embryonic and not well developed. The great amount of smooth muscle is explained as a sort of work hypertrophy. The great number of cysts which are unable to discharge their contents enlarge and cause a corresponding stimulus to the growth of smooth muscle.

CASE XI. Tumor occurred in a young man, and had perforated the scrotum before extirpation. Measures 6 cm. in diameter. Spermatic cord and epididymis normal. The tumor is surrounded by the tunica albuginea, and at the upper pole remains of testicular tissue are apparent beneath the albuginea. The tumor has arisen within the testicle. It is compact in consistency, smooth in outline, and on section shows a few large spaces surrounded by a great number of cysts of various sizes and shapes. These are supported by a stroma of connective tissue in which are here and there islands of cartilage.

*Microscopic.*—The testicular tissue at the periphery of the tumor is normal; in places it is in direct connection with the tumor; in places separated by a capsule formed of compressed testicular tissue. Areas of necrosis are present, due to thrombosis of the vessels. The connective tissue is often myxomatous and is arranged about cysts and glands. The great number of round and spindle cells suggests a sarcoma. Cartilage with perichondrium is present, and at opposite poles of the tumor the islands are connected to form a kind of cartilaginous skeleton. A large amount of striated muscle is present, occurring in many places. Cells with radial or concentric striations in the protoplasm and often containing multiple nuclei are present. (Wilms does not discuss these further.) Smooth muscle is also abundant. Squamous epithelium is present as in the above cases as solid nests, or as lining for cysts. Papillae of connective tissue are often found beneath. No attributes of the skin are found. Cylindrical epithelium lines cysts and canals. Goblet cells are sometimes present. Glands are located around the cysts and empty into them.

CASE XII. Patient 21 years old. Three years before observation pain in the left testis began and a small swelling was noticed. A slight trauma to the affected testis occurred two years later, and the growth increased rapidly in size. Extirpation of the testis followed and it was found to be the seat of a new growth.

The specimen measured 10 x 5 x 6 cm. and was completely surrounded by the tunica albuginea and tunica vaginalis. The spermatic cord, and its blood vessels, and the epididymis show no macroscopic changes. The surface of the tumor is smooth with the exception of two crescentic elevations located one at each pole. On section testicular parenchyma is found beneath the tunica albuginea in the region covered by epididymis. The main mass is cystic and in appearance resembles the normal testis, which is the seat of a carcinomatous or adenomatous new growth. No definite line of demarcation between the tumor and the remaining testicle tissue can be made out. Six nodules surrounded by capsules are found. Their structure is typical of teratoma, and they are in communication with the main tumor by means of fine canals penetrating the capsule. The interstitial tissue is in the form of bundles and contains much smooth muscle. Cartilage is also present and in one quadrant of the tumor is the predominant element.

*Microscopic.*—Spermatic cord, epididymis and vessels normal. The tissue of the testicle that remains shows distinct spermatogenic and sustentacular cells, although spermatogenesis has ceased. The tissue adjacent to the tumor is somewhat

degenerated. From this testicular tissue the main mass of the tumor seems to have originated. It has an alveolar arrangement, a connective-tissue stroma supporting it. The alveoli are filled solid with cells and have the appearance of carcinomatous tissue. Within the main tumor are located the six nodular growths above described, which have the typical structure of teratomata. Connective tissue of embryonic type often growing concentrically about blood vessels after the manner of angio-sarcomatous tissue is present. Myxomatous tissue is very prevalent about islands of cartilage and appears to be developed from it. Bone is present, developing directly from the connective tissue, and also from the cartilage. Smooth muscle is very abundant, but striated muscle is present only in the teratomatous nodule. Cysts and spaces lined by a mucous membrane of columnar and goblet cells represent the endoderm. Squamous epithelial elements represent the ectoderm. Epithelial pearls are often present, and by their growth seem to have stimulated the connective tissue about them to the formation of giant cells. In some instances spaces are surrounded by giant cells, the epithelial pearl evidently having undergone complete degeneration. Cells resembling the interstitial cells of the testis are found throughout the tumor, and seem to have undergone proliferation.

Gessner reports three cases:

CASE XIII. Patient 48 years old. A tumor the size of a goose-egg is located in the right testis. Growth has been accompanied by pain during previous ten months. The tumor is surrounded by the tunica vaginalis and a fibrous capsule. The growth passes over into the epididymis, and the testicle and epididymis as such are no longer recognizable. On section many cysts are present; the largest are the size of a hazelnut, with muco-serous or pulpy contents. Islands of cartilage can be seen and also numerous areas of necrosis infiltrated with blood. The cysts are in some instances lined by cubical epithelium. Structures which represent an intestinal anlage are numerous. Cysts containing epidermoidal elements are also present and often contain epithelial pearls. The interstitial tissue is composed of fibrillated connective tissue, elastic tissue, cartilage and smooth muscle. Blind canals lined by cylindrical epithelium changing to low endothelioid cells suggests strongly lung tissue. Large cells surrounded by spindle-shaped nuclei bear a close resemblance to ova.

CASE XIV. Patient aged 32; has had for five months a growth in the right testicle, which now is the size of the fist. The tunica vaginalis and some remains of the testicle surround the tumor. On section the tumor consists of numerous cysts, some as large as a hazelnut. Communication between cysts is frequent. Definite islands of cells occur in places, either solid or with lumen. Cysts having a lining either of cylindrical cells with formation of crypts or goblet cells, or ciliated epithelium, are present. Cysts with epidermoidal elements are also present. Alveolar glands are noted in some portions. The interstitial tissue is composed of connective tissue, either white fibrous or mucoid. Abundant smooth muscle occurs. Elements of the peripheral and central nervous system, glia cells, ganglion cells and nerve fibres are found. Nodules are found in the nervous tissue surrounded by connective tissue, and contain osteoblasts with a deposit of calcareous salts. The veins of the spermatic cord are dilated and thrombosed. Some thrombi have a connective tissue membrane and contain cells resembling osteoblasts. Other thrombi contain nervous tissue elements, nerve fibres and cells, and ganglion cells.

CASE XV. Patient, aged 33 years. Tumor of testicle three-fourths size of the fist and egg-shaped. A capsule with smooth surface surrounds the tumor. The testicle and epididymis as such are no longer recognizable. On section a few small spaces and canals are noted but no large cysts. There is a bony area the size of a berry located in the substance of the growth.

*Microscopic.*—The main mass of the tumor is carcinomatous. There are canals lined by cylindrical epithelium, often with villi. A few canals with squamous epithelial lining are noted. The nodule of bone has a definite periosteum and a marrow cavity with osteoblasts. Cartilage with a perichondrium, smooth muscle and connective tissue of a cellular or myxomatous character forms the stroma. Cysts are present containing ganglion cells, the latter in some cases surrounded by epithelial-like cells.

Case reported by Coley and Buxton.<sup>3</sup>

CASE XVI. Patient 27 years old. A slight enlargement of the right testis was observed eight months before operation. No history of trauma. Physical examination revealed a tumor the size of an orange, symmetrical and firm. No enlargement of inguinal glands.

*Pathological Examination.*—Tumor about the size of an orange; testis forms a cap over upper pole. The whole is enclosed in the tunica vaginalis. The tumor also has a special fibrous capsule from which the testis can easily be removed. On section the tumor is made up of tough semi-translucent material containing minute cysts. Elements of all three germinal layers are present. The ectoderm is represented by epidermoidal cysts with no development of skin attributes. The mesoderm is represented by smooth muscle, mucoid and cellular connective tissue, and hyaline cartilage with beginning ossification. The endoderm is present as irregular villous cysts lined by columnar epithelium. In the wall of these are fibrous connective tissue and smooth muscle. Masses of swollen hyaline cells, packed in alveoli and in close connection with endodermal cysts may represent the chorda dorsalis. The endodermal elements greatly outnumber the ectodermal elements.

LaGrange<sup>4</sup> reports a case as follows:

CASE XVII. Patient's right testicle larger than left. No cause given. It is about the size of a hen's egg. Following extreme fatigue a large tumor in the abdomen was noticed situated near the umbilicus. At the same time the testicle grew rapidly to double the original size. Patient could not say whether the tumor of the abdomen preceded or followed the one in the testicle.

*Autopsy.*—The testicle is now the size of an orange, hard, heavy and in certain parts is of a cartilaginous consistency. In shape it is pyriform and with smooth surface. Both layers of the tunica vaginalis are bound together. The epididymis and the remains of the testicular parenchyma are no longer recognizable as such. On section the tumor is of a white color with reddish striations. Islands of cartilage can be seen. No cysts are visible to the naked eye. The tumor in the abdomen extends three fingers breadth above the umbilicus; measures 32 x 38 cm., and weighs 8 kilos. It is hard and resistant above, soft and cystic below. On section the cysts are found to be as large as hens' eggs. The stroma is arranged in whorls and cartilage can be felt as sharp points. In the mesenteric glands is found tissue similar to that found in the abdominal tumor.

<sup>3</sup>Coley and Buxton, *Annals of Surgery*, September, 1901.

<sup>4</sup>LaGrange, *Bull. Soc. Anat. de Paris*, 1881, lvi, 100-106.

*Microscopic.*—The tumor of the testicle contains cysts which are lined by cylindrical and squamous epithelium. The stroma consists of connective tissue and cartilage. The latter has become impregnated with calcium salts. Sarcomatous tissue is abundant and surrounds the cartilage in some places. The tumor of the testicle is reproduced in the mesenteric lymph glands and in the large tumor above described.

Case reported by T. V. Jackson.\*

CASE XVIII. Patient aged 40 years. No family history of syphilis or tuberculosis. Tumor of the testicle removed at operation.

In gross appearance the tumor is massive, weighs 1 pound, is not resistant, and contains no fluid. No isolated masses of cartilage are seen. No involvement of glands in the inguinal region is present.

*Microscopic.*—Composite tumor congenital in origin. Stroma of connective tissue in which are bands of smooth muscle and islands of cartilage. Cysts are present lined by ciliated columnar epithelium, or by laminated epithelium which is undergoing keratoid change. Giant cells are present which resemble those of tuberculosis, although they may be of the nature of phagocytes (foreign body giant cells?).

The patient made a recovery, but later developed hæmoptysis, which was due to metastases to the lungs. Death resulted. No autopsy reported.

Case reported by Wm. F. Hendrickson.†

CASE XIX. Patient aged 25 years. The layers of the tunica vaginalis are bound together by adhesions. Two dome-like excrescences and a yellowish nodule represent tumor tissue, which is growing through the tunica vaginalis, and suggest that the adhesions may be due to tumor tissue. On section the dome-shaped excrescences are made up of a spongy network of blood vessels in a pinkish tissue.

*Microscopic.*—Cysts lined by stratified squamous epithelium are present and keratohyaline degeneration has occurred. A stroma of fibrous connective tissue contains hyaline cartilage and is infiltrated with polymorphonuclears and small round cells. Giant cells of foreign body type are present adjacent to cartilage. The dome-shaped tumors under the microscope are made up of a network of blood vessels, in the walls of which there has been a marked proliferation of epithelioid cells. The larger vessels have a perivascular growth which is papillomatous. Branches from the main vessel extend outward in a radiating manner, the connective tissue forming a papilla between each branch. The branching vessels are surrounded by perivascular new growth. An adrenal-like structure is also met with in the form of elongated masses of cells simulating those found in the cortex of the adrenal, and containing yellowish granules. The nuclei are deep staining and eccentrically placed. Lymphoid and plasma cells also present.

Case reported by Kockel.‡

CASE XX. Child aged 3½ years. Congenital tumor of the right testicle. Consists of three parts: (a) solid portion; (b) small cystic portion; (c) large cystic portion. The whole tumor is encapsulated, and within the capsule the testicle is compressed. The epididymis and vas deferens are normal.

\*Jackson, T. V., *Lancet*, London, 1900, ii, 86-126.

†Hendrickson, Wm. F., *Univ. of Pennsylvania Medical Bulletin*, August, 1901.

‡Kockel, *Festschrift für B. Schmidt*, 1896, 153-171.

*Microscopic.*—The solid portion contains tissue of the central nervous system. Glia, nerve fibres, ganglion cells, and corpora amylacea which have undergone calcification. Hair, cartilage and bone are also present. Small cystic portion: Cysts surrounded by connective tissue lined by elements of epidermis, hair follicles surrounded by foreign body giant cells, and sebaceous glands occur. Cysts lined by cylindrical epithelium, glands of Lieberkühn, goblet cells and having a mucosa with muscularis mucosa are also present. Lymph nodules, islands of hyaline cartilage, connective tissue, fat, bone spicules and tissue resembling striated muscle are found. Large cystic portion. This is lined by epidermis. At one point the epithelium is cuboidal, with hair follicles and sebaceous glands. Smooth muscle occurs in the wall. The arrangement of the tissues suggests anlage of both the trachea and intestine.

Case reported by Lovett and Councilman.§

CASE XXI. Child three weeks old. Enlargement of scrotum noticed at birth, now the size of hen's egg. Considered a hydrocele on right side. Tumor grew rapidly and was removed at operation.

In gross appearance tumor was smooth in outline and occupied the region of the testicle. It measured 7 x 5 cm. The epididymis can be distinctly made out. On section tumor is seen to be made up of a stroma containing cartilage, within the meshes of which are many cysts. The largest of these measures 1 cm. in diameter.

*Microscopic.*—The cysts are lined by a variety of epithelial types, stratified squamous, simple low cuboidal, ciliated columnar, etc. Tissue containing pigmented epithelium resembles parts of the eye. Epithelial cells with oval nuclei and granular layer resemble the cones of the retina. The pigment granules are located between the cells. In the stroma is a large amount of striated muscle, cartilage, both hyaline and fibrous, and bone. The connective tissue resembles sarcomatous growth in places.

About seven months later a tumor grew in the right parietal region and seemed to have been pushed up through the skull. An exploratory operation was done but the growth was so extensive that it was deemed impossible to remove it. The cranium steadily increased in circumference at the rate of 1 cm. per day. Death soon followed.

At autopsy the tumor was found to have originated between the dura mater and the cranial bones. There were no adhesions between the dura and pia mater. The skin covering the tumor externally was not involved.

By microscopic examination, in addition to the usual derivatives of the three germinal layers, were found central nervous tissue. There was no differentiation into white and gray matter. Cells of Purkinje and nerve fibres were present. Striated muscle was also present, and aggregations of nuclei which are interpreted as muscle-plates.

Case reported by Robertson.¶

CASE XXII. Patient aged 49. The tumor located in left testis was first noticed four months previous, and since has progressively increased in size. The growth was not accompanied by pain. The testicle was uniformly enlarged and on section the parenchyma is found to be largely replaced by fibrous connective tissue and cartilage. The whole tumor is enclosed within the thickened tunics of the testicle.

On microscopical examination numerous cysts are found

§Lovett and Councilman, *Journal of Experimental Medicine*, 1897, ii.

¶Robertson, *Proceedings of the Path. Soc. Phil.*, 1899, Dec., p. 36.

which are in some instances lined by columnar epithelium of simple or stratified variety; in other instances lined by squamous epithelium. These cysts are surrounded by layers of smooth muscle. The stroma is made up of myxomatous and fibrous connective tissue, hyaline cartilage, fat tissue and smooth muscle.

#### Case reported by Hayden.<sup>10</sup>

CASE XXIII. Patient 27 years of age. There is no family history of tuberculosis, malignant disease or syphilis. The patient, however, gives a history of two gonorrheal infections, and with the second one a right sided epididymitis. The right testis since has been slightly larger than the left. Two and a half months previous to admission the right testis began to increase in size and was accompanied by some pain. The right half of the scrotum on examination was found to be occupied by a smooth, painless, heavy and elastic tumor. The epididymis and testicle could not be differentiated. The scrotum was not adherent. No involvement of the glands could be made out. At operation the tunica vaginalis was normal in appearance. The cord was not thickened.

The pathologic report showed the tumor to be mostly made up of sarcomatous and carcinomatous elements. The sarcomatous elements consisted of small round cells, spindle cells and a few giant cells. The carcinomatous elements were arranged as in an adenocarcinoma. Some mucous cysts were noted. The stroma consists of smooth muscle, fibrous connective tissue and nodules of cartilage in which beginning ossification was noted.

#### Case reported by Schwarz.<sup>11</sup>

CASE XXIV. Patient aged 28. Seven months previous to admission to the clinic the patient noticed a swelling of the left testicle. The tumor increased in size gradually, causing no discomfort. The tumor was punctured, but only a little blood was obtained.

In the left side of the scrotum an oval tumor can be made out on palpation. At the lower pole a soft mass is felt which has the shape of the testicle. The spermatic cord and epididymis can also be differentiated. Several lymphatic glands the size of a bean can be palpated in the inguinal region. After removal the tumor is seen to be about the size of the fist, and is covered by the tunica vaginalis and tunica albuginea. Only the globus minor of the epididymis is unchanged. The remainder is much compressed. On section the tumor has a lobulated structure. In the septa between the nodules are cystic spaces. The lobules between the septa are composed of a soft myxomatous tissue, which is often of a yellowish-brown color (probably due to hemorrhage), and small islands of cartilage. Cysts are also present near the surface, lined by epidermis and containing desquamated epithelium and cholesterol crystals.

Microscopic examination shows that the cysts are lined partly by cylindrical epithelium in one or more layers, partly by cubical epithelium, and partly by epithelium so much flattened that it resembles endothelium. No attributes of the skin are present. Epithelial pearls are often found in the cysts lined by squamous epithelium. Polygonal epithelial cells deeply pigmented and arranged in two irregular masses resemble the pigment epithelium of the retina. The stroma consists of embryonic connective tissue (which has grown so rapidly that it resembles sarcomatous tissue), fibrous connective

tissue, smooth muscle, hyaline cartilage, bone and lymph follicles. The blood supply is carried on by means of numerous blood vessels and spaces. They are so numerous in some places as to suggest an angioma. The arrangement of the smooth muscle, cartilage and cysts lined by cylindrical epithelium is such as to represent an anlage of the respiratory tract. Cysts with villus-like ingrowths of the cylindrical epithelial lining, surrounded by smooth muscle, represent an intestinal anlage.

#### Case reported by Schlagenhauser.<sup>12</sup>

CASE XXV. Patient is 43 years old. The tumor is located in the left testicle and measures 11 x 8 cm. It is covered by a dense connective-tissue capsule 1 mm. in diameter. Septa extend inward from the capsule and divide the tumor into lobules. The parenchyma of the testicle and the epididymis are no longer recognizable. On section the tissue is brownish-red in color near the periphery, and grayish-red in the center. It is very friable. In the more fibrous portion cysts can be seen, either empty or containing a white glistening material. The structure bears a close resemblance to a decidua maligna of the uterus. A secondary growth is found in the lung about the size of a nut and sharply circumscribed from the surrounding tissue.

Microscopic examination shows elongated flattened spaces lined by one or more layers of cylindrical epithelial cells. The spaces lined by stratified squamous epithelium contain in the center an epithelial pearl. Spaces lined by a single layer of cylindrical epithelium are filled with the products of secretion. Tissue corresponding to embryonic lung, lymph follicles, smooth muscle and fibrous connective tissue is present. These elements, however, form a very small part of the tumor. The predominating tissue is composed of two varieties of cells closely associated with one another, and arranged to form irregular bands or circular structures and extend into spaces filled with blood. These masses have broken through into spaces lined by endothelium, or have grown along under the endothelial lining, thus elevating it. Within the lumen of a blood space at one point a tumor mass appears adherent to the endothelium; at another point a portion of the tumor appears free within the lumen. A study of the individual cells shows two types as above stated.

a. Masses of dark colored protoplasm, without cell division and multinucleated. The protoplasm is frequently vacuolated and contains leucocytes. No mitotic figures can be seen.

b. Polyhedral cells with light-colored protoplasm, heaped upon one another, without intercellular substance. The protoplasm is scant near the nucleus and contains glycogen. The nuclei are spherical with distinct chromatin network.

The former type is syncytium, the latter type Langerhans' cell layer. An examination of the metastatic growth in the lung shows only the syncytial cells and cells of Langerhans' cell layer arranged as in the primary tumor.

#### Case reported by Breuss.<sup>13</sup> Re-examined microscopically by Schlagenhauser.

CASE XXVI. Patient is 40 years old. Six weeks previous to examination a painful swelling in the scrotum was noticed. At the same time pain in the right half of the body and dyspnea developed.

By physical examination a hard tumor was found in the right testis. There was also dullness and râles over the lungs, a weak heart impulse, a loud double murmur at the apex, and tender-

<sup>10</sup> Hayden, American Med., May, 1902, p. 811.

<sup>11</sup> Schwarz, Inaugural Dissertation, Königsberg, 1900.

<sup>12</sup> Schlagenhauser, Wiener klinische Wochenschrift, May, 1902.

<sup>13</sup> Breuss, Wiener medicinische Wochenschrift, 1878.

ness over the abdomen. Later vomiting, dyspnoea and icterus developed, the tumor meanwhile increasing in size. Exitus after four weeks.

At autopsy the right testicle was found to be the seat of a tumor larger than the fist and nodular. On section cystic spaces were found filled with a yellowish or brownish fluid, and separated from one another by compact septa. The veins about the cord were the seat of a secondary growth, which could be traced continuously through the vessels of the spermatic plexus, right internal spermatic vein, inferior vena cava to the right auricle. There were no adhesions to the walls of the vessels. The growth in the right auricle extends both through the tricuspid orifice into the right ventricle, and through the open foramen ovale into the left auricle and ventricle. The growth within the heart consisted of finger-like processes with transparent yellowish lobules with cloudy opaque centers. The metastatic growth in the lung resembled in all respects that found in the heart.

*Microscopic Examination.*—The tumor in the testicle is composed of bands of myxomatous and fibrous connective tissue, and between these, nests of sarcomatous and carcinomatous tissue and cysts lined by cylindrical and cuboidal epithelium and goblet cells. The secondary growth within the veins and heart are composed of a myxomatous tissue covered by a layer of epithelial cells. At times divisions between these cells can be made out, but long masses of multinucleated protoplasm are also present. "The form, staining reactions, of the multinuclear syncytial masses and polygonal epithelial cells correspond closely to the epithelium of the chorionic villi." This case is interpreted by Schlagenhauser as a hydatidiform mole.

The following summary regarding this class of tumors is based on a study of our own cases and those reported in the literature.

*Structure.*—The gross appearance depends upon the proportionate development of the elements which make up the tumor. The tumors are generally cystic, and when distended with secretion the consistency is firm. At other times the consistency is soft and fluctuating. Resistant areas are often made out on palpation, due generally to the presence of cartilage or bone. The surface of the tumor may be smooth, or where nodules of solid tumor or cartilage are present, irregular. The epididymis and vas deferens are in most cases not involved, although the size of the tumor may mask their presence. On section the cystic structure can generally be made out with the naked eye, and a definite cyst lining is in some cases distinct. Papillary ingrowths are often present. The cyst contents vary. They may be mucilaginous, colloid-like, serous, or sebaceous. Hair has been found in some cyst cavities. Supporting the cystic structure is a stroma for the most part appearing as connective tissue, in which islands of cartilage can often be seen as minute, pearl-colored, translucent areas.

*Microscopic Appearance.*—Elements of the three primary germinal layers are constantly present except in Case IX, where no derivative of the ectoderm was found, but Wilms could not say positively that it was absent, since the whole tumor was not sectioned. Derived from the endoderm we find cysts or spaces with a lining of plain or ciliated columnar epithelium. Sometimes this is in a single layer,

sometimes it is stratified. Goblet cells and gland alveoli may occur. The inner surface of the cyst may be smooth or may be thrown into papillae with intervening crypts. Derived from the ectoderm we find epidermal elements in the form of a lining for cysts, or as solid processes. Degeneration often takes place in the solid processes, giving rise to cyst formation. The cells are often arranged as in the skin with all the different layers represented. An epithelial pearl frequently occupies the cavity of a cyst. Hair and sebaceous glands are rarely present, but were reported in connection with Case XX. Elements of the cerebral and peripheral nervous system were present in Cases XIV and XX. They are rarely present. The mesoderm is abundantly represented in most cases. Connective tissue, myxomatous and compact, smooth muscle and cartilage are the most constant elements. Bone was present in Cases III, XIV, XV, XVI, XX, XXI, XXIII and XXIV. Striated muscle occurred in Cases III, XI and XXI. The development of the circulatory system in the tumors varies. In some cases areas are found composed of nothing but blood vessels, as in Cases XIX (Hendrickson) and XXIV (Schwarz); then again only a few blood channels are found, as in Case I. In none of the above cases except Hendrickson's and Schwarz's were well developed blood vessels mentioned. The circulation seems to be carried on in many cases by channels lined by endothelium running within the stroma. Frequently the connective tissue is very cellular, and histologically has all the appearance of sarcomatous tissue. Giant cells of foreign body type are often present. They are arranged around epithelial pearls (Case XII), cartilage (Case XIX), and hair follicles (Case XX). Cells closely resembling ova surrounded by spindle-shaped nuclei are described in Case XIII. The arrangement of these different tissues is often such as to suggest the anlage of some organ. The rudimentary trachea and intestine are most frequently represented. In Case XIII Gessner found spaces lined by cuboidal epithelium with blind offshoots where the epithelium became flat. He was of the opinion that it represented the anlage of the lung. A similar anlage is noted by Schlagenhauser in Case XXV. In Cases XXI (Lovett and Councilman) and XXIV (Schwarz) tissues representing the anlage of the eye were described.

The three germinal layers do not develop equally, but the ectoderm and mesoderm are always in excess of those of the endoderm.

The large majority of these tumors develop in adults. Wilms was able to collect only four cases of undoubted congenital teratoma, to which should be added the cases reported by Lovett and Councilman, and Kockel. In the above twenty-six cases the age is given in only seventeen. In all but two (the congenital cases) it ranged between twenty-one to fifty years. There were eight cases in the third decade, two in the fourth, and seven in the fifth.

*Etiology.*—No explanation has shown satisfactorily why these tumors develop in adults. Traumatism has been reported in a few cases, but the clinical history has been so

rarely given that reliable data on this point are not obtainable. In only five instances in the above twenty-one cases was the presence or absence of traumatism stated. In Case III trauma occurred fifteen years previous to the development of the tumor. In Case XII trauma occurred two years after the growth had been noted. In Cases I and XVI absence of traumatism is definitely stated. In none of the above cases therefore could the growth of the tumor be directly or indirectly attributed to traumatism.

*Origin.*—Among the theories which have been advanced to explain the origin of these tumors are the following:

1. *The Theory of Metaplasia.*—It is assumed that one variety of tissue can change into another. Cysts were supposed to originate from the epithelium of the tubules in the testis, or from solid processes of cells derived from the tubules, the central portion degenerating, thus forming a cyst. This activity on the part of the epithelium was supposed to exert a stimulus on the connective tissue, which gave rise to the formation of cartilage, bone, etc. In cases where cartilage was found to antedate the cysts its development was supposed to stimulate the growth of epithelium. Ciliated epithelium was traced back to the remains of the Wolffian body. This theory does not admit of the possibility that all the elements of the tumor have a common origin. It is not accepted at the present day.

2. *Fœtus in Fœtu.*—Advanced by Meckel. This theory assumes that two ova are impregnated, both develop, one finally overpowering and enclosing the other.

Klebs divides the teratomata into—

(1) Endogenous—which result from the infolding of tissues during development.

(2) Ectogenous—which develop from a fetal implantation.

He further subdivides the ectogenous form into—

(a) Allantoid variety, in which the rudimentary fœtus develops in one of the body cavities of the other.

(b) Pre-allantoid, in which there is a complete or partial fusion of the two germinal areas, one becoming enclosed in the other.

Klebs states that in the allantoid variety a placenta and umbilical cord are found, while in the pre-allantoid variety they are absent. Wilms says of this theory that no organ of the principal fœtus could contain such a rudimentary parasitic fœtus, although it might well account for teratoid tumors in the body cavities. We could not explain Case II by this theory, since it would of course belong to the pre-allantoid variety yet has placental tissue in it.

3. *Theory of Cell Inclusion.*—This is a more recent theory advanced by Bonnet,<sup>14</sup> and assumes that either a fertilized polar body or that after the impregnation of the ovum, and during the early segmentation period, a cell or group of cells becomes separated and incorporated among the structures, which later develop into the testis. That such a separated segmentation cell even up to the sixteen-cell stage has the

power of developing into a fœtus has been proven experimentally in animals by Roux, Wilson, Hertwig and others. Barker notes that "Roux has noticed isolated segmentation cells in the body of young frog larvæ, and suggested that they might be of significance in the etiology of tumors." We do not know, however, the exact method by which such a cell could be included within the testis.

4. *Development from Cells Normally Present in the Testis.*—Wilms has shown conclusively that these teratomata arise in the rete testis, and has endeavored to trace their origin back to the true cells of the organ. He believes the tumor grows within the tubules and in proof of this points out that in one of his cases he found teratoid tissue in the adenomatous tissue of the tumor, and has also found it in a normal tubule. Growth within the tubules explains, as he believes, the cork-screw-like growth of the gland alveoli and the cyst formation. Malassez, on the other hand, believes the growth begins in the interstitial tissue, and cites instances where normal testicular tubules were found within the tumor. Wilms explains this fact by development within the tubules, the tumor by pressure shutting off some tubules and preventing growth into them. If the tumor develops within the tubules we have only the spermatogenic cell as a point of origin, since the sustentacular cell is not a germinal element. If it arises in the interstitial tissue Wilms suggests that it might originate in some way from the so-called interstitial cells of Leydig since Nussbaum believes these to be undeveloped germ cells. This view as to their significance, however is not unquestioned. How either the spermatogenic or the interstitial cell can develop into a teratoma is not known, and Wilms gives no explanation further than to say that the germ cell may have been pathological from the beginning or normal at first, later becoming pathological.

5. *Partial Hermaphroditism.*—Assumes the presence of an ovum in the testis, which after fertilization develops into a fœtus. This theory does not explain the tumors present at birth, or developing shortly after.

In discussing the relative merits of these theories we must consider the conditions which are to be explained. We have to explain the origin of a tumor which constantly contains derivatives of all three germinal layers, grows in the rete testis and in the majority of the cases develops in adult life. The theories of metaplasia, of fœtus in fœtu (since Kockel notes a case of teratoma in both testicles of the same individual), and of partial hermaphroditism do not explain these conditions, therefore may be discarded. We do not know how a spermatogenic cell could by itself give rise to a teratoma, and we do not know that Nussbaum's theory as to the significance of the interstitial cells is correct. The cell inclusion theory seems to be the most plausible, but leaves much to be explained. We cannot apply the results of experimental teratology on the lower animals to the human being. We cannot explain definitely how a segmentation cell can be included in the testis.

The occurrence of syncytial and decidual-like cells is noted in Cases II, XXV and XXVI.

<sup>14</sup> Bonnet, Monatschrift für Gynäkologie, Bd. xiii.

In Case II we cannot say positively whether we are dealing with true decidual cells or some other type of cell which resemble them. The cell type in question is, however, so closely associated with the syncytial cells that we are forced to conclude that they are either decidual cells or cells derived from Langerhans' cell layer, probably the latter.

Regarding the histogenesis of these cells there is still considerable difference of opinion, and it does not come within the scope of this paper to discuss the subject in detail. Briefly, however, it may be said that while Minot, Gottschalk, Kastschemke and others believe that both the syncytium and Langerhans cell layer are derived from the foetal ectoderm, Langerhans, Kossman and Merrtens believe the syncytium to be derived from the epithelium of the endometrium, and the cells of Langerhans layer from the foetal ectoderm. If the latter view is correct then we must assume the presence of an anlage of the uterus in these tumors. No tissue, however, was found which was interpreted as such. If both the syncytium and Langerhans' cell layer are foetal ectoderm then they should be classed with the proper elements of the tumor. Schlagenhauser believes both varieties of cells are foetal in origin. He expresses his belief that the cells of fertilized ovum or polar body destined under normal conditions to form placental tissue give rise to the syncytial cells and cells of Langerhans layer. Furthermore, he believes that the Langerhans' cell layer can develop into syncytium and frequently observed such a transition in his specimens. The presence or absence of placental epithelium in teratomata depends, according to Schlagenhauser's view, upon whether a fertilized cell in a comparatively early or late stage of development suffered inclusion. If placental epithelium is present he assumes that the tumor originated from a fertilized polar body; if absent, it originated from a blastomere.

*Malignancy.*—In Case V of Wilms series, tumor masses were found in the veins of the pampiniform plexus, which on section were cystic. Microscopically all three germinal layers were represented.

Case XIV, Gessner. The veins of the spermatic cord were thrombosed by tissue, which contain nerve cells, nerve fibres, ganglion cells and osteoblasts. All these were present in the primary tumor.

In Case XVII, reported by La Grange, a teratoma of the right testis was followed after extreme fatigue by a tumor of the abdomen, which microscopically corresponded to the growth in the testis.

In Case XXI, reported by Lovett and Councilman, we find a teratoma of the testis, which after removal was followed by a similar tumor of the cranial cavity. No connection between the two is claimed, since to metastasize, a portion of the tumor would have to be transplanted from the testis to the cranium. This is extremely improbable, especially as there were no metastases in the lungs or other internal organs.

In Case XXV (Schlagenhauser) a secondary growth was found in the lungs, which microscopically was found to be composed of syncytial cells and cells of Langerhans' layer

arranged in the same manner as those found in the primary tumor.

In Case XXVI (Schlagenhauser) a continuous growth could be traced within the vessels of the spermatic plexus to the heart. Macroscopically the growth was fungoid in character; composed of finger-like processes. Microscopically the structure of the secondary growth was composed of myxomatous tissue covered by syncytial cells and cells of Langerhans' layer.

The presence of the placental epithelial elements in the metastases but not in the primary tumor is explained by the fact that within the vessels these elements have a better physiologic environment for development (Schlagenhauser).

From these instances we must conclude that teratomata are sometimes malignant. The metastases, however, differ from those of carcinoma and sarcoma in that they cannot be due to the transplantation of individual tumor cells (except where only one type of tissue is represented in the secondary growth), but rather to a continuous growth of the teratoma, or to a transplantation of a small portion of it.

Can the individual elements of a teratoma, the stroma and the epithelium undergo a malignant change? In nearly every one of the cases reported above some portion of the tumor when examined microscopically suggested malignancy, and in many cases the original diagnosis was that of malignant tumor. But we cannot depend upon the microscopic picture alone to decide this point, inasmuch as the appearance of embryonic and malignant tumor tissue is so nearly alike. Clinical evidence must also be taken into consideration. The development of malignancy in the placental tissue of teratomata is believed by Schlagenhauser to be dependent upon the proliferating power of the cells. This in turn is dependent upon the inclusion of a fertilized cell in the earliest stages of development. "The earlier the inclusion in the development of the ovum, the higher the inborn power of the tumor cells to become clinically malignant." In Case V (Wilms) we have sarcomatous tissue penetrating the tunica albuginea and infiltrating the epididymis. It could not be determined, however, whether the sarcoma originated from the interstitial tissue of the testis or from the mesodermic elements of the teratoma.

Case XIX, reported by Hendrickson, of a teratoma testis showing perithelial angio-sarcomatous growth may be such a case. Adhesions between the tunica vaginalis were assumed to be metastases, but their microscopical structure was not given. There seems to be no way of determining whether this growth originated from the tissue of the teratoma. No clinical history is given. In Cases XXV and XXVI, however, this question is clearly answered in the affirmative. Since the placental epithelial elements in the metastases must have been derived from the embryonic elements of the tumor.

The presence of a malignant tumor of a testicle in which there was also a teratoma is illustrated by Case X of Wilms series. The greater part of the testicular parenchyma that

remains is normal, but that nearer the tumor shows the alveoli packed with cells. From this tissue the main mass of the tumor is derived and is of a carcinomatous nature.

In conclusion regarding malignancy we can say:

1. Teratoma can be malignant by growth along blood or lymph channels. The secondary growth being composed of derivatives of one or more of the three germinal layers.

2. Malignant new growth, originating from the tubules of the testis, and teratoma testis may exist simultaneously.

We are indebted to Dr. G. C. Madill, of Ogdensburg, New York, for the clinical history of Case I.

NOTE.—After this paper had gone to the press, we learned from Dr. Madill that his patient, Case I, shortly after the

attack of typhoid fever, had developed an abdominal tumor in the epigastric region.

The tumor increased rapidly in size and the patient became progressively weaker and died on September 5, 1902. A partial autopsy was performed and a tumor mass was found surrounding the head of the pancreas but not involving it.

Portions of the tumor tissue were removed and sent to us for diagnosis. Microscopic examination of the tissue showed that it was made up of cells irregular in shape and size, often containing budding nuclei.

The arrangement of the cells in places resembled that found in carcinoma but the greater part of the tumor was definitely sarcomatous.

## CORRESPONDENCE.

BERLIN, GERMANY.

*To the Editor:*—In THE BULLETIN February-March, 1902, Young described a modification of my prostatic incisor under the title of "A New Combined Electro-Cautery Incisor for the Bottini Operation for Prostatic Obstruction." According to him the chief advantage of this modification is, that knives of different heights may be used. Young believes to have brought out something new by this, but he is mistaken.

As proof of the above statement, I quote the following from my article of January-February, 1900, entitled: "Neue Mittheilungen zur Galvanokaustischen Radikalbehandlung der Prostatahypertrophie per vias naturales (Bottini'sche Operation)."<sup>1</sup>

"Theoretically the depth of the incision is represented by the height of the galvanocaustic knife, measured from its tip to the shaft at a right angle. It would seem, therefore, taking as an example the middle lobe, which may vary in size, to be an advantage, to have knives of different heights at our disposal. For this reason I had galvanocaustic knives made for me, measuring from 0.8, 1.0, 1.2 and 1.4 to 1.5 cm. I choose one of these, according to the cystoscopic finding, and, what is still more important, the rectal finding taken after the instrument has been introduced and turned backward."

I added the following note at the time (Footnote No. 17):

"As a rule, my instruments are manufactured with a knife of 1.2 cm., which represents the height mostly used, 0.8 cm. seems to me to be dispensable; 1.4 to 1.5 cm. is too high for many cases and has this further disadvantage, that the tendency to bend is naturally greater because of the increased height. It need only to be mentioned that the incision can be deepened by recutting in the incision either during the same sitting or at a later one."

I treated on the same question in my article on "The Treatment of Hypertrophy of the Prostate Gland by the Galvanocaustic Method after Bottini," in W. H. King's "Electricity in Medicine and Surgery." It may be found on p. 206, and is as follows:

"The depth of the incision is dependent, on the one hand, on the fact that the instrument be firmly pressed upon the prostate gland; on the other hand, on the height of the knife. I possess knives of various sizes, from 0.8 to 1.5 cm. in height, and choose between them dependent on the thickness of the prostate gland. As an average size 1.2 cm. is to be designated; my instruments are supplied with this size unless another size is especially ordered. The incision may also be deepened if the instrument is firmly pressed down and the knife is moved to and fro for a second time, along the furrow. In general, however, this is not expedient."

To be sure, I did not have an entirely new instrument made for each different knife; with my instrument, different male parts alone are necessary, the female remaining the same. The only difference between this and Young's is, that in his, a part of the outer end of the male portion remains the same. It is a question if there is any advantage in his arrangement, because the expensive part of the instrument is the platinum-iridium knife, of which one must have several in either case. The disadvantage of Young's is that the male part is made up of two pieces whereby it suffers in simplicity and safety.

In addition, I wish to emphasize that, as my experience increases, I have become convinced that knives of different heights are not of the great significance which I formerly thought, but one averaging 1.2 to 1.3 cm. in height is sufficient for all cases.

I may be allowed, as substantiation of this, to state that in my last 37 cases, as far as I can remember, all—or, at least, nearly all—were operated with a knife of 1.2 cm. height and in these 37 cases (excepting one death, one non-success in a

<sup>1</sup> Deutsche Medizinal-Zeitung, No. 1-6, 1900.

case with a small prostate, and one case which was operated too recently to allow of any opinion on the result) there were 34 successful results, 27 cases being cured and 7 decidedly improved.

At all events, from the above given quotations it is shown that the instrument recommended by Young can not be designated as "A New Electro-Cautery Incisor," but at most as a modification of mine. I must add that Young himself, in a letter to me, correctly recognizes this. He writes (March 24, 1902): "The instrument in question is merely a modification of your own splendid instrument."

ALBERT FREUDENBERG, M. D.

Berlin, S. W. Wilhelmstr. 20.

#### REPLY OF DR. YOUNG.

When I published the article entitled "A New Combined Electro-Cautery Incisor," I used the word "new" to designate a combination, which was and is an essentially novel plan. Although I had read numerous articles by Dr. Freudenberg I had failed to see the one in which he had spoken of employing more than one blade in his operations, else I should have referred to it. I had sent for his instrument and it was furnished with one blade, and in none of the subsequent catalogues of the German instrument-makers have I seen any reference to there being but one instrument and that with a single blade of given height.

I have now operated on over 70 cases of prostatic hypertrophy, and in this series have encountered the greatest variation in such hypertrophy as to size, shape, and consistence. In some the enlargement was as great as an orange; in others there was no enlargement at all, a mere sclerosis or fibromatous metaplasia, with little or no increase in size. Several cases of the latter type, where I feared to use Freudenberg's instrument lest the blade might cut too deeply, brought forcibly to my mind the need of blades of different sizes, small for very small prostates, medium for the usual enlargement, and large for great hypertrophies.

I wrote in March, 1901, to a prominent importing house in New York to ask if Freudenberg's instrument could be furnished with blades of different sizes, and received a negative reply. I then decided to have several blades constructed, similar in every way to the male blade of his instrument, each with the large screw traction wheel and axle firmly attached to it (as it now appears Dr. Freudenberg had done).

Realizing that such a combination would form a most cumbersome and unwieldy "set," I decided to substitute a simple mechanism whereby each blade might be easily detached from the traction apparatus, so that the latter would do for all blades. In the meantime, other defects in Freudenberg's

instrument had been detected which have in part been described in the paper in *THE BULLETIN* (q. v.) and changes were made to obviate them. In the end the following additions and alterations were made:

1. Four blades were constructed, .8, 1.2, 1.7, and 2.1 cm. high, which could be interchanged by the mere elevation of a "spring catch."

2. The mechanism of the connecting handle was radically changed so as to do away with the defective contact and overheating of Freudenberg's instrument.

3. The shaft was made so as to allow longer incisions for the great hypertrophies.

4. The beak was changed from the gentle slope, which frequently slipped into the urethra during the operation with unpleasant results, to a more rectangular shape, which effectually prevents such catastrophes.

5. The male blade was enlarged and changed so as to better carry a larger current, and the mechanism of attaching the platinum blades to the shaft was improved and strengthened.

6. The tedious screw which held the traction apparatus to the female blade was replaced by a quick-working "bayonet lock," thus greatly facilitating the change of blades and the cleansing of the instrument.

Other minor alterations were also made, but those I narrated seemed to justify the title "new," which was intended to apply to the combination and not to the single instrument itself, which I frankly stated was based on Freudenberg's model, the excellence of which I again acknowledge, as I did in the letter quoted by Dr. Freudenberg. A new instrument is not necessarily an entirely original one.

Dr. Freudenberg says that he now believes "that one blade is sufficient for all cases," that he has given up his "combination." We are not surprised that he has found it more agreeable to use his old instrument. With the "new" combined incisor, I find the ability to choose a blade to suit the size of the hypertrophy of the greatest value, and as the instrument has been used in now about 30 cases with perfect satisfaction, I can assure Dr. Freudenberg that his assertion that the improvement on his valuable incisor "suffers in safety" is incorrect, and, in fact, unwarranted (as he has never seen the instrument).

During the last year I have operated and cured with the small blade, several cases in which Freudenberg's instrument would probably have penetrated the prostatic capsule, and resulted fatally; and on the other hand, I have had success with the large blade in cases of great hypertrophy in which the 1.2 cm. blade, which Dr. Freudenberg now uses could not, I believe, have sufficiently cauterized for radical cure.

HUGH H. YOUNG.

Baltimore, July 13, 1902.

## NOTES ON NEW BOOKS.

The American Year-book of Medicine and Surgery for 1902. A yearly Digest of Scientific Progress and Authoritative Opinion in all branches of Medicine and Surgery, drawn from journals, monographs, and text-books of the leading American and foreign authors and investigators. Arranged, with critical editorial comments, by eminent American specialists, under the editorial charge of George M. Gould, A. M., M. D. In two volumes: Volume II, *General Surgery*. Octavo. 684 pages. Illustrated. (Philadelphia and London: W. B. Saunders & Co., 1902.) Per volume: cloth, \$3.00 net; half morocco, \$3.75 net.

The general scope of the Year-book is too well known to need any explanation. In this year's volume on surgery the first 363 pages, out of a total of 656 pages of reading matter, are devoted to general surgery; gynecology and obstetrics cover 170 pages, thus giving 533 pages for these major subjects. The remaining limited space is devoted to the specialties. Of the subjects which are discussed at considerable length we notice anesthetics, fractures, diseases of the respiratory and vascular systems, hernia, appendicitis, diseases of the liver. In the 363 pages of somewhat coarse print devoted to general surgery it is, of course, impossible to give anything like as adequate a review of the subject as is to be found in the standard German and French works of this character, such as *L'Année Chirurgicale* and *Hildebrand's Jahresbericht*, but very many valuable papers are abstracted at some length. As a digest of scientific progress and authoritative opinion drawn from American and foreign sources, the section devoted to surgery fails to meet our expectations. If the book claimed to be a discussion of the views of leading American writers it would be nearer the truth. The vast majority of the reviews are those of papers in the English language, which of course means that a large number of extremely important foreign papers fail to receive any notice whatever. As an example of this we may take the chapter on Surgical Diseases of the Liver. Thirty-two papers are abstracted and discussed. Of this number all but three are from papers printed in the English language, and twenty-three or over two-thirds are abstracts of papers by American writers. If the Year-book is to be made what it claims to be, a general review of the opinions of both American and foreign writers, this fault should certainly be corrected in future volumes, for not only is this true of diseases of the liver which we have taken as an example, but the preponderance of abstracts from American and English sources is equally striking in all subjects. The chapters devoted to gynecology and obstetrics show evidence of much wider reading and more careful selection of articles from the literature on the part of the editors of these chapters. This section of the book should prove of great value to both specialists and the general practitioner who desires a fairly complete review of latest opinions on these subjects. The chapters devoted to the specialties cover so little space that we fail to see how they can be of very great help to specialists, although they may be of some aid to general practitioners in calling attention to important topics. As an example of the very brief space allowed to the specialties, we notice that only ten pages are devoted to the entire subject of orthopedic surgery, in which branch there are so many active workers at present. Such reviews, grouping together the most important papers on various subjects in one volume, may be made of the greatest value, and we hope that the American Year-book may be improved in the future so as to compare favorably with similar publications in Germany and France.

## BOOKS RECEIVED.

*The Diagnosis of Surgical Diseases.* By Dr. E. Albert. Authorized translation from the eighth enlarged and revised edition by Robert T. Frank, A. M., M. D. With fifty-three illustrations. 1902. 8vo. 419 pages. D. Appleton & Company, New York.

*Atlas and Epitome of Operative Surgery.* By Dr. Otto Zuckerkandl. Second edition, revised and enlarged. Authorized translation from the German. Edited by J. Chalmers Da Costa, M. D. With 40 colored plates and 278 illustrations in the text. (Saunders' Medical Hand-Atlases.) 1902. 12mo. 410 pages. W. B. Saunders & Company, Philadelphia and London.

*Atlas and Epitome of Otology.* By Gustav Brühl, M. D., with the collaboration of Prof. Dr. A. Politzer. Authorized translation from the German. Edited by S. MacCuen Smith, M. D. With 244 colored figures on 39 lithographic plates, and 99 text illustrations. (Saunders' Medical Hand-Atlases.) 1902. 12mo. 292 pages. W. B. Saunders & Company, Philadelphia and London.

*A Practical Manual of Insanity.*—For the Medical Student and General Practitioner. By Daniel R. Brower, A. M., M. D., LL.D., and Henry M. Bannister, A. M., M. D. 1902. 8vo. 426 pages. W. B. Saunders & Company, Philadelphia and London.

*A System of Physiologic Therapeutics.* Edited by Solomon Solis Cohen, A. M., M. D. Volume VI.

*Dietotherapy and Food in Health.* By Nathan S. Davis, Jr., A. M., M. D. 1901. 8vo. 372 pages. P. Blakiston's Son & Co., Philadelphia.

*Diseases of the Intestines.* Their Special Pathology, Diagnosis, and Treatment. By John C. Hemmeter, M. D., Philos. D. Volume II. Appendicitis, Tuberculosis, Syphilis, Actinomycosis of Intestine, etc. With plates and many other original illustrations. 1902. 8vo. 679 pages. P. Blakiston's Son & Co., Philadelphia.

*Saunders' Pocket Medical Formulary.* With an Appendix containing Posological Table; Formulae and Doses for Hypodermic Medication; Poisons and their Antidotes, etc. By William M. Powell, M. D. Sixth edition, thoroughly revised. 1900. 16mo. 297 pages. W. B. Saunders & Company, Philadelphia.

*University of Pennsylvania. Contributions from the William Pepper Laboratory of Clinical Medicine.* No. 2. (Reprints.) 1901. Philadelphia.

*Syphilis.* A Symposium. Special Contributions by L. Duncan Bulkley, A. M., M. D.; Pollen Cabot, Jr., M. D.; Louis A. Duhring, M. D. 1902. 12mo. 120 pages. E. B. Treat & Company.

*Diseases of Women.* A Manual of Gynecology. Designed Especially for the Use of Students and General Practitioners. By F. H. Davenport, A. B., M. D. Fourth edition, revised and enlarged. With 154 illustrations. 1902. 12mo. 405 pages. Lea Brothers & Company, Philadelphia and New York.

*Manual of Child-bed Nursing.* With Notes on Infant Feeding. By Charles Jewett. Fifth edition, revised and enlarged. 1902. 12mo. 84 pages. E. B. Treat & Company, New York.

*The International Medical Annual.* A Year-book of Treatment and Practitioner's Index. Twentieth year. 1902. 12mo. 688 pages. E. B. Treat & Company, New York.

- 1 Laboratory Guide in Elementary Bacteriology.* By William Dodge Frost, M. S. Second revised edition. Illustrated. 1902. 8vo. 355 pages. Published by the Author, Madison, Wisconsin.
- Transactions of the College of Physicians of Philadelphia.* Third series. Volume the Twenty-third. 1901. 8vo. lxxii + 320 + 143 pages. Printed for the College, Philadelphia.
- An Introduction to Physiology.* By William Townsend Porter, M. D. Part IV, Physiological Optics. 1902. 12mo. 99 pages. The University Press, Cambridge, Mass.
- Ophthalmic Myology.* A Systematic Treatise on the Ocular Muscles. By G. C. Savage, M. D. Sixty-one illustrative cuts and six plates. 1902. 12mo. 589 pages. Published by the Author, 139 N. Spruce Street, Nashville, Tenn.
- Philadelphia Hospital Reports.* Volume IV. 1900. Edited by Roland G. Curtin, M. D., and Daniel E. Hughes, M. D. 1901. 8vo. 324 pages. Philadelphia.
- The Operations of Surgery.* Intended Especially for the Use of those Recently Appointed on a Hospital Staff and for those Preparing for the Higher Examinations. By W. H. A. Jacobson, M. Ch. Oxon., F. R. C. S., and F. J. Steward, M. S. London, F. R. C. S. Fourth edition. With five hundred and fifty illustrations. Two volumes. 1902. 8vo. P. Blakiston's Son & Company, Philadelphia.
- The Principles of Bacteriology.* A Practical Manual for Students and Physicians. By A. C. Abbott, M. D. Sixth edition, enlarged and thoroughly revised. With 111 illustrations, of which 26 are colored. 1902. 12mo. 641 pages. Lea Brothers & Co., Philadelphia and New York.
- The Climates and Baths of Great Britain.* Being the Report of a Committee of the Royal Medical and Chirurgical Society of London. C. Theodore Williams, M. D., Chairman; P. Horton-Smith, M. D., Hon. Secretary. Volume II—The Climates of London and of the Central and Northern Portions of England, Together with those of Wales and of Ireland. 1902. 8vo. 628 pages. Macmillan & Company, Limited, London; The Macmillan Company, New York.
- Diseases of the Nose, Pharynx, and Ear.* By Henry Gradle, M. D. Illustrated. 1902. 8vo. 547 pages. W. B. Saunders & Company, Philadelphia and London.
- Quain's Dictionary of Medicine.* By Various Writers. Third edition, largely rewritten and revised throughout. With fourteen colored plates and numerous other illustrations. Edited by H. Montague Murray, M. D., F. R. C. P., assisted by John Harold, M. B., B. Ch., B. A. O., and W. Cecil Bosanquet, M. A., M. D., M. R. C. P. 1902. 8vo. 1892 pages. D. Appleton & Company, New York.
- Nothnagel's Encyclopedia of Practical Medicine.* Diphtheria. By William P. Northrup, M. D. Measles, Scarlatina, German Measles. By Theodor von Jürgensen, M. D. Edited, with additions, by William P. Northrup, M. D. Authorized translation from the German, under the editorial supervision of Alfred Stengel, M. D. 1902. 8vo. 672 pages. W. B. Saunders & Company, Philadelphia and London.
- The Clinical Pathology of the Blood.* By Dr. Rud. R. v. Limbeck. Translated from the second German edition by Arthur Latham, M. A. (Oxon. et Cantab.) M. R. C. P. Lond., and John Nachbar, M. A., M. D. Cantab. 1901. 8vo. 333 pages. The New Sydenham Society, London.
- Anatomy in its Relation to Art.* An Exposition of the Bones and Muscles of the Human Body, with Especial Reference to their Influence upon its Actions and External Form. By George McClellan, M. D. Illustrated by three hundred and thirty-eight original drawings and photographs made by the author and expressly prepared for this work. 1901. 4to. W. B. Saunders & Company, Philadelphia and London.
- Medical Lectures and Aphorisms.* By Samuel Gee, M. D. 1902. 16mo. 296 pages. Smith, Elder & Company, London.
- A System of Physiologic Therapeutics.* Edited by Solomon Solis Cohen, A. M., M. D. Volume IX, Hydrotherapy, Thermotherapy, Heliotherapy, and Phototherapy. By Dr. Wilhelm Winternitz, assisted by Dr. Alois Strasser and Dr. B. Buxbaum, and Balneology and Crounotherapy, by Dr. E. Heinrich Kisch. Illustrated. 1902. 8vo. 570 pages. P. Blakiston's Son & Co., Philadelphia.
- Atlas and Epitome of Traumatic Fractures and Dislocations.* By Prof. Dr. H. Helferich. Authorized translation from the German. Edited by Joseph C. Bloodgood, M. D. Fifth edition, revised and enlarged. With 216 colored illustrations on 64 lithographic plates and 190 figures in the text. (Saunders' Medical Hand-Atlases.) 1902. 12mo. 353 pages. W. B. Saunders & Company, Philadelphia and London.
- Transactions of the Medical Association of Georgia.* Fifty-third Annual Session. 1902. 8vo. 486 pages. Published by the Association, Atlanta, Ga.
- The Medical Annual.* A Year-book of Treatment and Practitioner's Index. Twentieth year. 1902. 12mo. John Wright & Co., Bristol; Simpkin, Marshall, Hamilton Kent & Co., Ltd., London.
- Report Relating to the Registration of Births, Marriages and Deaths in the Province of Ontario for the year ending 31st December, 1900.* Printed by order of the Legislative Assembly of Ontario. 1902. 8vo. 61 + ccxvi pages. L. K. Cameron, Toronto.
- Fifteenth Annual Report of the State Board of Health of the State of Ohio.* For the year ending October 31, 1900. 8vo. 603 pages. [1901] Columbus, Ohio.
- Psychopathological Researches.* Studies in Mental Dissociation. With text figures and ten plates. Boris Sidis, M. A., Ph. D. 1902. 8vo. 329 pages. G. E. Stechert, New York, London, Leipzig, Paris.
- Selected Essays and Monographs, Chiefly from English Sources.* Braxton Hicks; Bodington; Hodgkin; Paget; Humphry; Ehlers. With Obituary Notice of the Society's Late Treasurer, Dr. Sedgwick Saunders. 1901. 8vo. 325 pages. The New Sydenham Society, London.
- The Mental Functions of the Brain.* An Investigation into their Localisation and their Manifestation in Health and Disease. By Bernard Hollander, M. D., M. R. C. S., L. R. C. P. (London). Illustrated with the Clinical Records of Eight Hundred Cases of Localised Brain Derangements and with Several Plates. 1901. 8vo. 507 pages. G. P. Putnam's Sons, New York and London.
- Gibson and Russell's Physical Diagnosis.* Third edition revised and rewritten by Francis D. Boyd, C. M. G., M. D., F. R. C. P. Ed. With 144 illustrations. 1902. 12mo. 448 pages. D. Appleton & Company, New York.

*Treatise on Diseases of the Skin.* For the Use of Advanced Students and Practitioners. By Henry W. Stelwagon, M.D., Ph.D. With 220 illustrations in the text, and 26 full-page lithographic and half-tone plates. 1902. 8vo. 1115 pages. W. B. Saunders & Company, Philadelphia and London.

*A Manual of Instruction in the Principles of Prompt Aid to the Injured.* Including a Chapter on Hygiene and the Drill Regulations for the Hospital Corps, U. S. A. Designed for Military and Civil Use. By Alvah H. Doty, M.D. Fourth edition, revised and enlarged. 1902. 12mo. 302 pages. D. Appleton & Company, New York.

*Applied Surgical Anatomy.* Regionally Presented. For the Use of Students and Practitioners of Medicine. By George Woolsey, A. B., M.D. With 125 illustrations, mostly colored. 1902. 8vo. 521 pages. Lea Brothers & Company, New York and Philadelphia.

*A Treatise on Diseases of the Anus, Rectum and Pelvic Colon.* By James P. Tuttle, A. M., M.D. With eight colored plates and three hundred and thirty-eight illustrations in the text. 1902. 8vo. 961 pages. D. Appleton & Company, New York.

*Diseases of the Stomach.* Their Special Pathology, Diagnosis, and Treatment, with Sections on Anatomy, Physiology, Chemical and Microscopical Examination of Stomach Contents, Dietetics, Surgery of the Stomach, etc. By John C. Hemmeter, M.D., Philos. D. With many original illustrations, a number of which are in colors, and a lithograph frontispiece. Third enlarged and revised edition. 1902. 8vo. 894 pages. P. Blakiston's Son & Company, Philadelphia.

*The Principles and Practice of Bandaging.* By Gwilym G. Davis, M.D. Illustrated from original drawings by the author. 1902. 8vo. 146 pages. P. Blakiston's Son & Company, Philadelphia.

*Practical Dietetics.* With Special Reference to Diet in Disease. By W. Gilman Thompson, M.D. Second edition, enlarged and thoroughly revised. 1902. 8vo. xxiii + 828 pages. D. Appleton & Company, New York.

*Minor Surgery and Bandaging.* Including the Treatment of Fractures and Dislocations, the Ligation of Arteries, Amputations, Excisions and Resections, Intestinal Anastomosis, Operations upon Nerves and Tendons, Tracheotomy, Intubation of the Larynx, etc. By Henry R. Wharton, M.D. Fifth edition, enlarged and thoroughly revised, with 509 illustrations. 1902. 12mo. 621 pages. Lea Brothers & Company, Philadelphia and New York.

*The Diseases of the Nose, Throat and Ear.* By Charles Prevost Grayson, A. M., M.D. Illustrated with 129 engravings and 8 plates in colors and monochrome. 1902. 8vo. 540 pages. Lea Brothers & Company, Philadelphia and New York.

*Twenty-fifth Annual Report of the Board of Health of the State of New Jersey and Report of the Bureau of Vital Statistics, 1901.* 8vo. 459 pages. 1902. Trenton, New Jersey.

*A Guide to the Practical Examination of Urine.*—For the Use of Physicians and Students. By James Tyson, M.D. Tenth edition, revised and corrected. With a colored plate and wood engravings. 1902. 12mo. 297 pages. P. Blakiston's Son & Company, Philadelphia.

*Die Röntgenstrahlen im Dienste der Chirurgie.* Von Dr. Carl Beck. 1902. 8vo. 138 pages. [I. Teil, Text; II. Teil, Tafeln.] Seitz & Schauer, München.

*Physical Diagnosis.* Diseases of the Thoracic and Abdominal Organs. A Manual for Students and Physicians. By Egbert Le Fevre, M.D. Illustrated with 74 engravings and 12 monochrome plates. 1902. 12mo. 448 pages. Lea Brothers & Company, Philadelphia and New York.

*Practical Diagnosis.* The Use of Symptoms and Physical Signs in the Diagnosis of Disease. Fifth edition, revised and enlarged. By Hobart Amory Hare, M.D., B.Sc. Illustrated with 236 engravings and 25 plates. 1902. 8vo. 698 pages. Lea Brothers & Company, Philadelphia and New York.

*General Paresis.* Practical and Clinical. By Robert Howland Chase, A. M., M.D. Illustrated. 1902. 8vo. 291 pages. P. Blakiston's Son & Company, Philadelphia.

*The Diseases of Infancy and Childhood.* For the Use of Students and Practitioners of Medicine. By L. Emmett Holt, M.D., LL.D. Second edition, revised and enlarged. With two hundred and twenty-five illustrations, including nine colored plates. 1902. 8vo. D. Appleton & Company, New York.

*The Diseases of Infancy and Childhood.* Designed for the Use of Students and Practitioners of Medicine. By Henry Koplik, M.D. Illustrated with 169 engravings and 30 plates in color and monochrome. 1902. 8vo. 675 pages. Lea Brothers & Company, New York and Philadelphia.

*The International Text-book of Surgery.* By American and British Authors. Edited by J. Collins Warren, M.D., LL.D., Hon. F.R.C.S. Eng., and A. Pearce Gould, M.S., F.R.C.S. Second edition, thoroughly revised. Volume I, General and Operative Surgery; Volume II, Regional Surgery. 1902. 8vo. W. B. Saunders & Company, Philadelphia and London.

*A Text-book of Surgical Principles and Surgical Diseases of the Face, Mouth and Jaws.* For Dental Students. By H. Horace Grant, A. M., M.D. Illustrated. 1902. 8vo. 231 pages. W. B. Saunders & Company, Philadelphia and London.

*A Text-book of Materia Medica, Therapeutics and Pharmacology.* By George Frank Butler, Ph.G., M.D. Fourth edition, thoroughly revised. 1902. 8vo. 896 pages. W. B. Saunders & Company, Philadelphia and London.

*The Treatment of Fractures.* By Charles Locke Seudder, M.D. Third edition, thoroughly revised. With 645 illustrations. 1902. 8vo. 455 pages. W. B. Saunders & Company, Philadelphia and London.

*Essentials of Histology.* By Louis Leroy, B.S., M.D. Arranged with Questions following each Chapter. 92 illustrations. Second edition, revised and enlarged. 1902. 12mo. 263 pages. (Saunders' Question-Compends, No. 25.) W. B. Saunders & Company, Philadelphia and London.

*Essentials of the Diseases of the Ear.* Arranged in the Form of Questions and Answers. Prepared Especially for Students of Medicine and Post-Graduate Students. By E. B. Gleason, S.B., M.D. Third edition, thoroughly revised. 1902. 12mo. 214 pages. (Saunders' Question-Compends, No. 24.) W. B. Saunders & Company, Philadelphia and London.

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# BULLETIN

OF

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## THE HUXLEY LECTURE

ON

### RECENT STUDIES OF IMMUNITY WITH SPECIAL REFERENCE TO THEIR BEARING ON PATHOLOGY.

*Delivered at the Opening of the Winter Session of Charing Cross Hospital Medical School on October 1, 1902.*

By WILLIAM H. WELCH, M. D., LL. D.

*Professor of Pathology, Johns Hopkins University, Baltimore.*

You will readily believe that with my deep appreciation of the high honor conferred by the invitation to deliver the fourth Huxley lecture there was joined a sense of great embarrassment in being called upon to follow in this office three such leaders of world-wide fame as Sir Michael Foster, Professor Virchow, and Lord Lister. But the letter of the committee of the Charing Cross Hospital Medical School stated that the choice of a successor to these great names was "a tribute of our admiration for the great army of scientific workers on the other side of the Atlantic." While I cannot assume to occupy any other place in this army than that of a soldier in the ranks, I felt that if my acceptance of this invitation could be regarded as in any sense an expression of appreciation by American workers in science of the commendation and good will of our British colleagues, of our large indebtedness to them, of our sense of the common interests, the comradeship and the kinship of the English-speaking peoples on both sides of the ocean, I should not decline, even if summoned to occupy a position of danger.

There was another consideration which I may be permitted here to mention. Through Huxley there is, if not a bond, at least a link between the Charing Cross Hospital Medical School and the Johns Hopkins University. This lectureship was founded to commemorate the fact that Huxley received his entire medical education at the Charing Cross Hospital Medical School. While throughout America the name of Huxley is held in high honor as that of a great discoverer and interpreter in science, and while the influence which he has exerted upon popular, as well as scientific opinion through those messages peculiarly fitted to the needs of English thought is not less there than among his own countrymen, we at the Johns Hopkins University have special reasons to acknowledge our gratitude to him. He crossed the ocean to deliver the principal address at the opening of this University in 1876, and he then gave utterance to ideas concerning university, and especially medical, education which were at the time and have remained an inspiration and a guide to us. Then, too, the Johns Hopkins University owes to Huxley and to Michael Foster the

accession to its faculty of my lamented colleague, Newell Martin, who by the introduction and development of the biological methods and conceptions of his teachers gave such new directions and so great an impulse to biological study in America that his own work and that of his pupils started for us a new era in this department.

The first Huxley lecturer has made it unnecessary for his successors to dwell upon Huxley's studentship at the Charing Cross Hospital, upon the important influence which this had upon his career, or upon his great services to medical science, although his chief title to fame lies outside of the domain of medicine. I should like, however, to quote a passage, although it must be familiar to you, from Mr. Leonard Huxley's charming "Life and Letters" of his father, which has appeared since the date of Sir Michael Foster's lecture, for it shows that "it was at Charing Cross Hospital where Huxley first felt the influence of daily intercourse with a really able teacher." He says: "No doubt it was very largely my own fault but the only instruction from which I obtained the proper effect of education was that which I received from Mr. Wharton Jones, who was the lecturer on physiology at the Charing Cross School of Medicine. The extent and precision of his knowledge impressed me greatly and the severe exactness of his method of lecturing was quite to my taste. I do not know that I have ever felt so much respect for anybody as a teacher before or since." Wharton Jones, who will doubtless be longest remembered as the discoverer of the amoeboid movements of the white blood corpuscles, was an experimental physiologist and pathologist of much originality, and it seems to me that there has not been, even in his own country, so full a recognition of his work as its importance merits.

Before passing to the special theme of this lecture it is fitting that I should pause, if only for a moment, to call to mind with affection and reverence that recently departed great man who honored and delighted you four years ago and who has conferred such high distinction upon the office of Huxley lecturer. When one considers the full import of the discovery and establishment by Virchow of the principles of cellular pathology, that these constitute the secure foundation upon which nearly two generations have built and future generations will continue to build the edifice of scientific medicine, I do not know what greater name there is in the whole history of medicine than that of Rudolf Virchow. How noble his character! With what amazing industry, versatility and keenness of intellect did he fruitfully cultivate the new fields which he had opened to research, as well as other departments of science! With what devotion and beneficial results did he give his time and abundant knowledge to the service of the public and of our profession! We mourn the loss of a hero of medicine and of science, a benefactor of his race, and we rejoice in the rich fruitage of a long and well spent life.

The first place in experimental medicine to-day is occupied

by the problems of immunity and, in accordance with the trust of the Huxley Lectureship, which provides that the lecture shall relate to "recent advances in science and their bearing upon medicine and surgery," I have chosen for my theme "Recent Studies of Immunity with special reference to their Bearing on Pathology." As it would be hopeless to attempt a complete review of this broad subject within the space of a single lecture, I shall dwell more particularly upon certain of its aspects, not always of necessity the most important ones, which I conceive to be less familiar to most physicians, or which have engaged my attention, although much which I shall say is of course known to those who have followed the results of recent work in these new lines of investigation.

Under "studies of immunity" I have included, as a matter of convenience, though not with strict accuracy, investigations, which, although the direct outgrowth of those primarily directed toward a solution of the problems of immunity, have extended far beyond these bounds, and have revealed specific properties of cells and fluids in health and in disease of the broadest biological interest. We find illustrated here the familiar fact, nowhere more important to recognize than in medicine, that the sciences are interdependent, that discovery in one field sheds light in the most diverse and often unexpected directions and opens new paths to research. We shall see also exemplified the fructifying influence upon the advancement of knowledge of the discovery and application of new methods of investigation.

In endeavoring to follow in its intimate workings the contest of the living body with its invaders the attention of investigators has naturally been drawn both to the action of the cells and to the properties of the fluids of the body in this struggle, to the latter sometimes without sufficient consideration of the dependence of the humors in their composition upon the cells. Each of these lines of study, whether followed separately or conjointly, has led to the discovery of important facts relating to the mechanism of immunity.

We owe to Metchnikoff and his pupils the most important observations concerning the direct participation of leukocytes and other cells in the processes of infection and the production of immunity. Whatever attitude one may take toward Metchnikoff's well-known phagocytic theory of immunity, one must recognize the wealth of new facts which he has brought to light, and must admire the skill and fertility of resource with which for two decades he has defended this theory against severe assaults, and he has done so, in my judgment, with a large measure of success. With wonderful ingenuity in his recent book on immunity he rescues the phagocytes and applies to a deeper insight into their activities results of his opponents' work.

The other line of research, in some respects more important, was opened by Nuttall in 1888, working in Flüggé's laboratory, by his systematic study of the antibacterial properties of the body fluids, particularly of the blood-serum. It is true that there were previous indications of the power of

fresh blood to kill bacteria; indeed, if one wishes to trace this matter historically to its roots, he must go back to John Hunter, who was quite familiar with the anti-putrefactive power of fresh blood, although of course he knew nothing of bacteria. Hunter showed that putrefying fluid could be added in small quantity to fresh blood without setting up putrefaction, and in elaborating his favorite doctrine of the "living principle of the blood" he interested himself greatly in certain phenomena which, interpreted in the light of our present knowledge, are clear anticipations of some recent findings.

After Nuttall our knowledge of the bactericidal power of blood-serum was extended by Buchner and others, but the next advance of fundamental importance in this direction was Pfeiffer's discovery in 1894 of the quick extracellular disintegration and solution of cholera spirilla in the peritoneal cavity of immunized guinea-pigs, or in that of normal guinea-pigs treated with immune serum, and of the presence in the immune serum of a specific substance concerned in the bacteriolytic process, although by itself without bactericidal power.

In the meantime Behring had made his great discovery of antitoxic immunity and of the protective and curative value of antitoxic serum, and Ehrlich had done much to elucidate the nature of this form of immunity. It soon became apparent, however, that immunity from the great majority of bacterial infections does not depend in the main upon the antitoxic principle. The attention of bacteriologists, therefore, was drawn more and more to the so-called "Pfeiffer phenomenon," which was found to be of great general significance, and starting from this and especially from the investigation of the analogous and much more readily studied solution of red corpuscles by foreign serum there has followed in rapid succession up to the present time a series of new and most interesting discoveries and conceptions with which are connected many names, but most prominently those of Metchnikoff and Bordet, and of Ehrlich and Morgenroth.

Through these various studies of immunity we have become acquainted with an important physiological capacity of the healthy organism, the extent and in most instances the existence of which was unsuspected until quite recent years. This capacity is the power to produce substances specifically antagonistic to all sorts of foreign cells and cellular products and derivatives. The substances capable of inducing this immunizing reaction appear to be mainly of an assimilable, albuminous nature, or at least intimately associated with such material, although it has been proved that certain non-albuminous derivatives of proteids have the same power.<sup>1</sup>

<sup>1</sup> Specific precipitins have been produced by injection of crystalline and other so-called pure proteids. Obermayer and Pick produced immune bodies by the use of non-albuminous products of tryptic digestion of certain albumins. Jacoby has shown that the specific body concerned in ricin immunization is non-albuminous. A. Klein obtained entirely nega-

The mode of antagonism of the specific bodies formed in response to the reception within the living organism of substances capable of inducing the necessary reaction varies with the nature of these latter substances, and consists in such diverse manifestations as neutralization of poisons and of ferments, injury or destruction of cells, associated with characteristic morphological changes, cessation of motility of cells or their appendages, agglutination of cells, precipitation and coagulation. In accordance with these different effects the corresponding antagonistic bodies, or anti-bodies as they are called, are classified as antitoxins, anti-enzymes, cytotoxins, agglutinins, precipitins, and coagulins, and even against these bodies, with the exception of the antitoxins, antagonists have in turn been produced. All of these bodies are in varying, but usually high degree specific with reference both to the nature and to the source of the material upon which they exert their characteristic effects.

The cytotoxins or cytolytins include not only the bacteriolytins and hæmolytins but also a great number of other cellular toxins present in the sera of animals which have received injections of cells from a different species. To every cellular group of an animal species there appears to correspond a specific cytotoxin. To designate these various cytotoxins such self-explanatory names as leukotoxin, spermotoxin, nephrotoxin, neurotoxin, thyrotoxin, syncytiotoxin are used. Their specificity extends not only to the nature of the cells but also to the species of animal furnishing the cells used for their production.

One of the most important results of recent work is the separation of these specific anti-bodies into two groups, in one of which, represented by the antitoxins, the antagonists are single bodies; while in the other, represented by the cytolytins, the antagonistic effect requires the cooperation of two bodies. Of these two bodies the one which actually destroys the foreign cells or induces other specific effect is normally present in the cells or fluids of the organism, but it seems incapable of action without the intermediation of a body which is distinguished from it by greater resistance to heat and which is produced by the immunizing reaction, although it may also be normally present in smaller amount.<sup>2</sup> The two elements composing a cytolytin exist quite independently of each other, so that one may be present without the other or be artificially removed without affecting the other. Of the multitude of names proposed for these cytolytic components, those most commonly used for the body

tive results with injections of starch, glycogen, glucose, gum arabic, and gelatine.

<sup>2</sup> Metchnikoff believes that the complement or cytase, which in his opinion exists under normal conditions solely within cells, not free in the plasma, acts in natural immunity without the cooperation of an intermediary body or fixative, the latter being concerned only in acquired or artificial immunity. The evidence seems, however, to favor the view that in this regard the conditions are similar in both forms of immunity, the main difference being the presence of a much larger amount of the specific immune body in the latter.

which is the specific product of immunization, although it may also exist normally, are intermediary body, immune body, amboceptor, sensitizer, fixative, preparative, copula, desmon, and for the other body complement, alexin, cytase. It is this latter body which contains the atomic group described as toxophoric or zymophoric.

Concerning the source, mode of action, and constitution of the specific antagonistic bodies we are very imperfectly informed. That they are of cellular origin seems certain and Ehrlich with great ingenuity on the basis of a brilliant series of experiments has advanced an hypothesis regarding them, which, in my opinion, better than any other hitherto suggested accords with the known facts and in promoting discovery has already done the greatest service of which a working hypothesis is capable. Ehrlich has so recently and so fully in the Croonian lecture presented before English readers his hypothesis of the side-chains or receptors and the basis for it, that I need only recall to your minds his conception that the toxins, cells and other substances which lead within the living body to the production of antitoxins, cytolytins, and other antagonists have this capacity only through the possession of specific affinities, called haptophore groups, for corresponding haptophore groups belonging to side-chains or receptors of certain cellular constituents of the body, and that, in consequence of this appropriation of receptors, others of like nature are reproduced in excess of the needs of the cell, and these being shed into the lymph and blood there constitute the antitoxins, intermediary bodies, agglutinins and other specific antagonists. The antitoxic receptor has only a single combining affinity, which is for the toxin; whereas the cast-off receptors constituting the intermediary bodies of cytolytins have at least two affinities (hence called amboceptors by Ehrlich), one of a more highly specialized nature being for the invading bacteria or other foreign cells, and the other for the complement.<sup>2</sup> The anti-body enters quantitatively into definite chemical union with its affinitive substance.

The essence of Ehrlich's theory concerning antitoxin is thus tersely expressed by Behring: "The same substance which, when incorporated in the cells of the living body, is the prerequisite and condition for an intoxication becomes the means of cure when it exists in the circulating blood." So of the twofold bactericidal and cytolytic agents we may

say that the living body possesses substances which may protect it by destruction of invaders or may injure it by destruction of its own cells according to the mates with which these substances are joined.

An inquiry which naturally arises in this connection is: What is the physiological mechanism called into action in the processes resulting in the production of antitoxins, cytolytins, and similar bodies? We have no reason to suppose that the animal body is endowed with properties specially designed to meet pathological emergencies. Its sole weapons of defense, often lamentably imperfect for morbid states, are adapted primarily to physiological uses.<sup>3</sup> To the foregoing inquiry Ehrlich answers that the mechanism concerned is one physiologically employed for the assimilation by the cells of food. The receptors are in the cells not for the purpose of linking poisons to the cells but to seize certain food-stuffs, particularly the proteids, and the toxins and bacterial and other foreign cellular substances, if capable of inducing the immunizing reaction, chance to have the requisite combining affinities for the food-receptors. It is interesting that Metchnikoff also, though from a different point of view, refers the mechanism of immunity to the physiological function of assimilation of food by the cells.

Inasmuch as according to Ehrlich's hypothesis the specific antagonistic substances resulting from the injection of toxins and of foreign cells or derivatives of cells exist preformed in cells of the normal body, there would appear to be no reason why anyone of them might not occasionally be present normally free in the blood or fluids. In fact many of them, such as diphtheria and tetanus antitoxins, various anti-enzymes, bactericidal, hæmolytic and other cellular toxins, agglutinins and a number of other bodies of this class, as well as their anti-bodies, have been found repeatedly, though of course in the case of many inconstantly and with marked differences between individuals and species, in the blood of healthy human beings or animals when their presence could not reasonably be attributed to a previous specific immunization. Of these normal anti-bodies the only one which is increased in amount by the process of immunization is that specifically related to the material used to bring about the reaction. As already stated it is the intermediary body,<sup>4</sup> not the complement, which is generated in immunization against bacteria and other cells.

The foregoing statements, though of necessity condensed and incomplete, about the general characters of the specific anti-bodies will, I trust, help to a better understanding of what is to follow concerning the bearing of some of these discoveries on medical science and practice. I realize the difficulties which you must already have experienced, if un-

<sup>2</sup> According to Ehrlich's latest conception resulting from investigations to demonstrate the multiplicity of complements an amboceptor has a single cytophilic affinity and a number of complementophilic affinities differing in their avidity for various complements. He regards the agglutinins, precipitins and coagulins as uniceptors of more complex structure than the antitoxins, but Bail has recently brought evidence to show that agglutinins, like cytolytins, are composed of two elements. For the purposes of this lecture it is not deemed necessary to enter into these or many other details of this complicated subject. For comprehensive and admirable critical reviews of recent theories of immunity and Ehrlich's hypothesis of the receptors I would refer to Dr. Ritchie's papers in "The Journal of Hygiene," Vol. II, Nos. 2, 3 and 4, and to Dr. Aschoff's paper in *Zeitschrift f. allgem. Physiologie*, Bd. I, Heft 3, Jena, 1902.

<sup>4</sup> W. H. Welch: *Adaptation in Pathological Processes*. Trans. Congress American Physicians and Surgeons, 1897, Vol. IV.

<sup>3</sup> I use in this lecture the name "intermediary body" in preference to the more technical term "amboceptor," although Ehrlich applies the German equivalent—*Zwischenkörper*—only to normal as distinguished from immune amboceptors.

familiar with these new lines of research, in following a brief presentation of a subject in which not only are the facts so complex and the ideas so novel, but the terminology so strange and burdened with such a multitude of confusing synonyms. While deploring the multiplication of unnecessary new terms, I should like to quote in this connection a wise remark of Huxley:<sup>6</sup> "If we find that the ascertainment of the order of nature is facilitated by using one terminology, or one set of symbols, rather than another, it is our clear duty to use the former; and no harm can accrue so long as we bear in mind that we are dealing merely with terms and symbols."

The most remarkable and characteristic attribute of these anti-bodies is the specificity of their relation to the substances which have led to their formation. Of some of them, such as diphtheria or tetanus antitoxin this specificity is nearly absolute; of others, such as the precipitins, it is only relative. This property is the basis of new and most valuable methods for the identification of species and the determination of genetic relations—species not only of living things, but also of chemical substances and of disease.

The resemblances and the differences thus revealed are doubtless fundamentally of a physico-chemical nature, but in many instances they transcend the powers of the microscope or of ordinary chemical tests to detect.

The results already attained by the method of serum diagnosis,<sup>7</sup> using this expression in its widest sense, are not only of interest and importance to the biologist, physiologist, and chemist, but of great practical value to the bacteriologist and the physician. As this is not an aspect of my subject, broad and important as it is, upon the details of which I propose to dwell, it must suffice to present by way of illustration examples of the diagnostic application of different kinds of specific sera.

The only certain means of detecting toxins of the class of diphtheria or tetanus toxin, snake venom, and certain vegetable poisons of the same category is their neutralization by the corresponding antitoxic sera. Occasion may arise where such detection is of practical and even medico-legal importance, as has been exemplified in India, where the criminal use of cobra venom is not unknown.

The application of serum diagnosis which is most familiar

to physicians is the agglutinative test for typhoid fever. The principles of the agglutinative reaction were worked out in the laboratory of Professor Gruber in Vienna by himself and Durham and were there first applied to the diagnosis of typhoid fever by Grünbaum, who was anticipated in his publication by Widal, who has made a thorough clinical study of the subject. The method is of great value not only in the diagnosis of disease but also in the identification of bacterial species and the recognition of relationships between species. Durham, to whom we owe important contributions to this subject, has given an ingenious hypothetical explanation of mutual agglutinative reactions, the main features of which are paralleled in Ehrlich and Morgenroth's doctrine, based upon experiments, relating to the multiplicity of cell-receptors and of amboceptors concerned in hæmolysis.<sup>8</sup>

We have found the agglutinative reaction an indispensable aid in the study of the series of cases of paratyphoid fever which have come under observation in Dr. Osler's wards at the Johns Hopkins Hospital, and which otherwise it would have been scarcely possible to have separated from typhoid fever.<sup>9</sup> The occurrence of paratyphoid fever as a distinct disease affords an explanation of a certain proportion of the failures of the serum from supposed typhoid-fever patients to clump typhoid bacilli. Not less valuable is the serum test in the diagnosis of *Bacillus dysenteriae* Shiga and of the diseases caused by it. This microorganism has been shown by Flexner and his pupils, Vedder and Duval, to be the cause of our acute dysenteries, and recently in Baltimore Duval and Bassett, working with the aid of the Rockefeller Institute for Medical Research at the Thomas Wilson Sanitarium, have discovered that this same bacillus is probably the specific agent of infection in the summer diarrhœas of infants.

Bacteriolytic sera have been used by Pfeiffer in the differentiation of cholera and allied spirilla, but few other bacteria present equally well the Pfeiffer reaction, which is not nearly so useful or handy a means of identification as the Gruber-Durham reaction.

Of other cytolytic sera the hæmolysins have been by far the most carefully studied. One of the most interesting results of this study has been the determination by precise quantitative methods of resemblances and of differences between red blood corpuscles which in no other way could be distinguished. These resemblances and differences relate not only to the red corpuscles of different species of animals, but also to those of individuals of the same species. Although we constantly assume the existence of cellular differences between individuals and between species, these are for the most part so subtle a nature as to elude our methods of observation. The exact demonstration of such differences

<sup>6</sup> Huxley: On the physical basis of life. Collected Essays, Vol. I, p. 164, New York, 1893.

<sup>7</sup> The general procedure followed in the production of specific sera is the injection into a suitable animal at intervals of time repeated doses of toxins, bacteria, foreign cells or other material against which the anti-body is desired. For example if a specific precipitating or a hæmolytic serum for human blood is wanted, an animal, say a rabbit, is injected subcutaneously or intraperitoneally at intervals of three or more days with five or six doses of human serum or human red blood corpuscles. At the end of this time the rabbit's serum has acquired the property of precipitating human serum in strong dilutions, or of dissolving human red blood corpuscles, if these were used for the injection. Within limits the less closely related the two species of animals, the more powerful is the antagonistic effect of the specific serum. This is true especially in the case of cytotoxic sera.

<sup>8</sup> Durham: Journal of Experimental Medicine, Jan. 15, 1901, Vol. V, p. 353. Ehrlich and Morgenroth: Berliner klin. Wochenschr., May 27, 1901, p. 670.

<sup>9</sup> See papers on paratyphoid fever by Johnston, Hewlett, and Longcope in American Journal of Medical Sciences, August, 1902.

by the use of cytolytic sera is, therefore, of especial interest. My assistant, Dr. H. T. Marshall, in an unpublished research, conducted under the direction of Professor Ehrlich and Dr. Morgenroth, upon the receptors of the red blood corpuscles of man and of two species of monkey found that while man and the monkeys each has receptors not shared by the other they also have a large number of receptors in common.

This result is in harmony with Nuttall's interesting observations on a much more extended scale regarding phylogenetic relationships between animal species as shown by the reaction of their blood with the specific precipitins discovered by Tschistowitch and Bordet and introduced into practical medicine by Wassermann. This biological test to determine the source of blood, when used with proper precautions, far surpasses in accuracy all other methods for this end. While it would lead too far from my purpose to follow this subject farther, I cannot in this connection forbear at least mentioning one of the earliest and most suggestive papers on this class of anti-bodies, that "On Immunity against Proteids" by Walter Myers, who gave up his life in the cause of science and of humanity and whose early death is so great a loss to English medical science.

I shall ask your attention now to some considerations concerning the bearing of recent studies of immunity on the nature and action of toxins. This subject is of course of the greatest pathological as well as bacteriological importance, and I believe a closer cooperation than now exists between bacteriologists and pathologists in its study would further the surer and more rapid advancement of our knowledge about it. One misses only too often in purely bacteriological papers on this subject exact knowledge and descriptions of pathological conditions, and on the other hand pathologists often fail to utilize pertinent facts and ideas which are familiar to bacteriologists.

The discovery by Roux and Yersin of the diphtheria toxin, the studies by Behring and Kitasato of tetanus toxin leading up to Behring's epochal discovery of antitoxin, and the later investigations of Ehrlich on the constitution of diphtheria toxin and the origin and mode of action of antitoxin are the great events in the most brilliant and securely founded chapter of modern studies of immunity. Through these researches we became acquainted with a class of poisons secreted by certain bacteria and present in solution in culture fluids. The evidence is conclusive that these soluble toxins enter, as assimilable substances, into direct combination with constituents of the body cells for which they have an affinity, and only thereby are enabled to bring about immunity or to exert toxic effects. As shown by the modifications of toxins called toxoids, the toxic property may be lost without loss of the combining power and without removal of the immunizing power. According to Ehrlich's helpful conception, based on a large amount of experimental evidence and now generally accepted, the combining power of the toxin molecule resides in a group of atoms, designated as the haptophore group, with affinity for the corresponding haptophore

groups of the side-chains or receptors of cellular constituents, and the toxic power pertains to another and less stable atom-complex in the molecule.

By means of these facts and legitimate deductions from them we are enabled to explain in a satisfactory way susceptibility to poisoning by these soluble toxins, their selective action upon the cells of the body, and their quick disappearance after injection into the circulating blood. In one infectious disease and in one only, to wit tetanus, are we able to explain the clinical and pathological phenomena in minute detail on the basis of our knowledge of the causative microorganism and its poisonous products. The nearest approach to this instance is diphtheria, but here we have not yet been able to follow the trail of the toxins within the body so perfectly, and, as Flexner and I have shown, in addition to the soluble toxins there is an intracellular poison concerned in the production of the false membrane. Interesting investigations, which have greatly helped to elucidate the nature of these toxins, have been made on various similar vegetable and animal poisons, such as ricin and abrin from the former source and the venom of snakes, spiders and other poisonous animals.

The high hopes which were raised by the discovery of the soluble bacterial toxins that at last the way was opened for us to penetrate into the mysteries of the mode of action of pathogenic bacteria were soon doomed to disappointment, for similar powerful toxins, though diligently sought, could not be detected in the cultures of most other bacteria, and these among the most important ones, such as the tubercle bacillus, the typhoid bacillus, the cholera spirillum, the pneumococcus, the pyogenic micrococci. This disappointment was all the more acute because there was and is every ground for confidence that whenever we have in our possession a powerful toxin of this class, a strong protective antitoxic serum can readily be obtained.

Notwithstanding these negative results the belief was not abandoned that bacteria harm the body mainly by poisoning, for it rests upon strong clinical and pathological evidence, as well as upon the study of the distribution of bacteria in the infected body. The search for poisons was turned from the fluid part of cultures to the bacteria themselves and thus Pfeiffer succeeded in demonstrating as an integral constituent of the bodies of cholera spirilla toxic substances, which are liberated only when the bacteria degenerate or die. Intracellular poisons, which indeed previously, though of a different nature, had been extracted from bacteria by Buchner and by Koch, were subsequently found within typhoid bacilli and a number of other pathogenic bacteria.

It is of more than purely bacteriological interest to recognize the distinction between the small group of pathogenic bacteria, represented by the bacilli of tetanus, of diphtheria, and of botulism, characterized by the secretion of powerful soluble toxins, and the much larger group, containing most of the other pathogenic bacteria, which do not secrete similar strong toxins, for it is only the former which give rise to

the production of antitoxic sera of marked protective and curative power.

The form of immunity resulting from injections or natural infections with the second class of bacteria belongs mainly to the bacteriolytic type, in which the complete anti-body is not a single substance, like antitoxin, but is composed of two distinct elements, intermediary body and complement, of which only the former is produced or increased in the process of immunization. The bacteriolytic sera are also under suitable, but not readily controlled conditions protective and curative, but owing, it would seem, mainly to the duplex nature of the anti-body their successful therapeutic application meets difficulties which have not yet been overcome. The great practical problem of bacteriology to-day is to make available to medical practice the bacteriolytic sera, such as anti-typhoid, anti-pneumococcus, anti-streptococcus, anti-plague, anti-dysentery sera. Such work as that of Marmorek, of Wassermann, of Neisser and Wechsberg, of Ainley Walker upon the production, the properties, the conditions underlying the action of these sera is, therefore, highly important.

Our knowledge of the constitution and action of the intracellular bacterial poisons is most incomplete and at present cannot be applied in any very definite and satisfactory way to the explanation of the morbid phenomena of infectious diseases. Such investigations as those undertaken by Macfadyen and Rowland at the Jenner Institute of Preventive Medicine upon the expressed juices of bacterial cells promise to shed light upon this subject and in general upon the vital processes of bacteria. The recent researches of Vaughan and his collaborators upon intracellular bacterial toxins are also most valuable.

I find it difficult to reconcile myself to the doctrine that bacteria such as the typhoid bacillus, the pneumococcus, and others of the class now under consideration do their chief injury to the body, not while they are lively and vigorous, but after they become corpses and in consequence set free their protoplasmic poisons. Still this latter conception is the basis of a coherent hypothesis of infection, elaborated most fully recently by Radziewsky,<sup>10</sup> which rests upon a considerable amount of accurate observation and interesting experimental work. There can be no doubt that in the course of many infections there goes on an enormous destruction of the bacteria concerned, so that the numbers of those indicated at any given time by microscopical examination and by cultures may represent only an insignificant fraction of the total progeny of the first invaders. I have been much interested in this phenomenon since I became familiar with it over twelve years ago<sup>11</sup> in pneumococcus infections through the employment of a method which revealed in the

exudates degenerating and dead pneumococci and their empty capsules in numbers often far exceeding the intact organisms, indeed in some cases so many that they formed a large part of the exudate.

While all due weight should be given to such facts as these the objections to the acceptance of the hypothesis just mentioned as affording a complete explanation of the toxic phenomena of this class of infections are so obvious that naturally efforts have been made to learn whether bacteria which produce no strong soluble toxins in our ordinary culture media may not do so on other media of special composition or in a demonstrable way within the living body. Work in these two directions has not been altogether barren as shown by results of experiments made by Hueppe, Cartwright Wood, Marmorek, and others, along the former lines, and by Metchnikoff, Roux and Salimbeni along the latter, but it cannot be said that these experiments have led to any generally accepted solution of the main difficulties. Some are therefore inclined to lay the chief emphasis upon disordered cellular metabolism, but this is only a restatement of the question. Everybody recognizes abnormal metabolism as an essential condition in infections. The very point needing explanation is how the bacteria derange metabolism.

I wish here to advance an hypothesis which seems competent to explain the source, the mode of production, and the nature of certain bacterial toxins. It would appear to be a natural inference from the receptor theory of Ehrlich and the recent work on cytotoxins. The following considerations will, I hope, make clear the essential points.

As I have already stated, we know that the injection of foreign cells, such as pathogenic bacteria, red blood corpuscles, spermatozoa, epithelium, into the tissues of a living animal leads to the formation of poisons, called cytotoxins, acting specifically upon these cells; that the substances which stimulate the cells of the host to produce one constituent of this class of toxins consist of certain atom-complexes derived from the injected cells; that certain cells of the host thus stimulated generate and discharge one component of the toxin, called the intermediary body, which becomes the medium of intoxication through union, on the one hand, with a pre-existent toxophore substance, called the complement, and, on the other hand, with the foreign cell which started the reaction.

Such is the response on the part of the host to the entrance of the foreign cells, but how about a possible response of a like nature on the part of the invading cells toward the host, resulting in the production of special cytotoxins, of analogous constitution, injurious to the host? This latter response, being of a vital nature, can take place only when the invading cells are living, as in the case of bacteria and other parasites. I see no reason why suitable substances derived from the host may not stimulate parasitic organisms through a physiological mechanism similar to that operative in the development of cytolytic immunity, to the production of intermediary bodies, which, if provided with the requi-

<sup>10</sup> Radziewsky: *Zeitschrift für Hygiene*, 1900, XXXIV, p. 369, and 1901, XXXVII, p. 1.

<sup>11</sup> Welch: *Bulletin of the Johns Hopkins Hospital*, July, 1890, and December, 1892. Michaelis (*Berliner klin. Wochenschr.*, 1902, No. 20) has recently reported similar findings.

site affinities, have the power to link complements to cellular constituents of the host and thereby to poison the latter. Expressed in terms of Ehrlich's side-chain theory, certain substances of the host of cellular origin, assimilable by the parasites through the possession of haptophore groups with the proper affinities, become anchored to receptors of the parasitic cell, which, if not too much damaged, is thereby stimulated to the over-production of like receptors; these excessive receptors of the parasite, if cast off into the fluids or the cells of the host, there constitute intermediary bodies or amboceptors with special affinities for those cellular constituents or derivatives of the host which led to their production and for others which possess in whole or in part identical receptors. Provided the host is supplied also with the appropriate complements there result cytotoxins with special affinities for certain definite cells or substances of cellular origin in the host. The contribution of the parasitic cells to these cytotoxins is the amboceptors. Either the parasite or the host may provide the complements.<sup>12</sup>

It may perhaps aid in grasping the ideas here presented to imagine the bacterium, in the capacity of the host, as a structure so large that one could inject into it animal cells. Provided the proper receptor apparatus is present, the resulting reaction on the part of the bacterium, as described, would be a process of immunization against the animal cells through the formation of specific celluicidal substances. In reality it is only certain atomic complexes of cells which are concerned in this immunizing reaction, and in comparison with these even the smallest bacterium is a gigantic object.

Looked at from the point of view of the bacterium, as well as from that of the animal host, according to the hypothesis advanced, the struggle between the bacteria and the body cells in infections may be conceived as an immunizing contest in which each participant is stimulated by its opponent to the production of cytotoxins hostile to the other and thereby endeavors to make itself immune against its antagonist. These mutually antagonistic cytotoxins are capable of injuring the parasitic cells, on the one hand, or the body cells, on the other, only when, escaping combination outside of them, they are anchored to the receptors of the cells to which their respective affinities are adjusted. This combination with the cells, if it does not result in too great injury to them, is the condition for further production of the cytotoxic intermediary bodies through overproduction and discharge of receptors.<sup>13</sup> The important factors deter-

mining the issue of the contest are the nature, the relative proportions and the distribution of the bacterial cytotoxins and the host's cytotoxins respectively.

The hypothesis thus outlined can be tested experimentally, but I regret that it has shaped itself in my mind so recently that I have not yet been able to make the desired experiments, which are, however, now started in my laboratory. Since my arrival here I am informed that these experiments have already furnished facts in its support.

Inasmuch as at least one component, and it may be both components, of the assumed bacterial cytotoxins preexist in the bacterial cells, it should be possible to demonstrate some of them in artificial cultures of bacteria, where they would be found especially as integral parts of the cells, unless extracted from the bodies of degenerating or dead bacteria. This corresponds with what is known concerning the situation of the poisons of the cholera spirillum, the typhoid bacillus, and other bacteria characterized by the lack of strong soluble toxins. But the quantitative and other relations between these cultural cytotoxins and those produced, in the manner described, by the same bacteria during processes of infection are comparable to those between the normal antibodies and the immune anti-bodies. These relations would explain the familiar fact that cultures of bacteria of the class under consideration constitute in general only a partial and meagre index of the toxic capacities of the same bacteria in the infected body. That cytolytic may, however, be present normally in large amount is illustrated by the hæmolysins of eel's serum and of snake venom.

and constitutes that atom group which causes the production of the immune body." My hypothesis includes the conception supported by Walker and also much more. According to the hypothesis certain antibodies of bacterial origin are capable not only of neutralizing immune bodies of the host but with the aid of complements also of poisoning the cells of the host. It is not difficult to imagine various conditions in which the anti-bodies of bacterial origin may escape neutralization before entering into union with the host's cells. The substances which stimulate bacteria to produce these anti-bodies need not necessarily be toxic to them; in fact toxicity, such as that of strong bactericides of cellular origin, would hinder their production. The essential things are that the stimulating substances have the requisite combining groups for bacterial receptors, and that the cast off receptors be complemented within the body of the host.

Each of the various bacteriogenic cytotoxins probably contains a multitude of partial amboceptors with varying cytophilic and complementophilic affinities, in accordance with the views of Ehrlich and Morgenroth.

It is self evident that through a mechanism similar to that described parasites within the infected body may be stimulated by atomic groups derived from the host to the production also of anti-bodies other than complex cytotoxins, such as various agglutinins, precipitins, anti-enzymes, and perhaps of uniceptors of the nature of secreted, soluble toxins, or of enzymes, all adjusted against the host.

Questions relating to the source and nature of the complements, particularly of intra-cellular complements, and also to anti-complements, are manifestly of importance in relation to the hypothesis, but it would complicate the subject too much to discuss these and other matters here, where my purpose is merely to outline the essential features of this new theory of infection with reference to the particular points under consideration.

<sup>12</sup> We may thus speak of somatogenic cytotoxins resulting from the action of bacterial stimuli on cells of the host, and of bacteriogenic cytotoxins from somatogenic stimuli, also of somatogenic and bacteriogenic complements.

<sup>13</sup> It will be observed that these discharged receptors may be regarded as the equivalents of anti-immune bodies. E. W. Ainley Walker, in an interesting and suggestive paper on "Immunisation against Immune Serum" (*Journal of Pathology and Bacteriology*, March, 1902), shows experimentally that bacteria growing in immune sera produce anti-immune bodies and thereby become more virulent. He concludes that "the basis of bacterial virulence and of chemiotactic influence is identical,

In this theory degenerated and dead bacteria, while recognized as a source of poisoning in infections, are not assigned an exclusive rôle in this regard. Living bacteria in the infected body, where they are under nutritive conditions not paralleled in artificial cultures, actively produce and secrete receptors which may become the means of intoxication of the body cells. From what has been said, we can comprehend how these diverse free receptors may enter into the formation of cytotoxins of the most varied and specific characters, such as erythotoxins, leukotoxins, neurotoxins, nephrotoxins, spermotoxins, hepatotoxins, etc. Very probably in many instances these toxins are represented by so few receptors in bacterial cells in ordinary cultures, that it would be hopeless to search for them there, although we may have convincing experimental and pathological evidence that within the animal body the same bacteria produce them abundantly under the stimulus of appropriate substances derived from cells of the host.

The methods hitherto employed for the study of bacterial poisons have not generally been calculated to reveal the presence of toxins with the characters indicated, even if such existed in the cultures. Recently, however, a beginning has been made in this direction, and we have already become acquainted with certain toxins of an interesting nature, to which I desire to direct your attention.

Intrinsically and in their general bearing upon the subject before us the recent investigations of Flexner and Noguchi upon the constitution of the toxins in snake venom are of especial importance. It was in snake venom that Weir Mitchell and Reichert first demonstrated the existence of that class of poisons often called, although with doubtful propriety, toxic albumins. Investigations of snake toxins are of peculiar interest for many reasons, not the least of which is their resemblance to bacterial toxins. The demonstration by Sewall of the possibility of active immunization from venom and the further studies by Calmette and Fraser of this phenomenon and especially of the protective and curative properties of antivenin are well known.

Until recently it has been generally held that the venom toxins resemble in molecular structure the diphtheria and the tetanus toxins in being single bodies with a combining or haptophore group and a toxophore group of atoms. The researches of Flexner and Noguchi, now in progress, of which only the first part has been published,<sup>14</sup> necessitate a quite different conception of the nature and manner of action of venom toxins than that previously entertained. I have followed with great interest the work of Professor Flexner on toxins, begun several years ago in my laboratory when he was my assistant and associate, and since continued along new lines in his laboratory at the University of Pennsylvania and I wish to acknowledge his generosity in permitting me to use

in this lecture certain unpublished results of his and Noguchi's investigations.

These investigations have shown that the toxic action of venom upon red blood corpuscles, leukocytes, nerve cells, and other cells is like that of the duplex cytotoxins already described; that is, it depends upon the combination of intermediary bodies contained in the venom, on the one hand with the animal cells for which these bodies respectively have affinities and on the other hand with corresponding complements contained, not in the venom, but in the cells or fluids of the animal acted on. For example, it is well known that the addition of venoms to fresh blood brings about the quick destruction and solution of the red corpuscles. If, however, certain venoms be added to red corpuscles which have been thoroughly washed with isotonic salt solution so as to remove all the complement, the corpuscles are agglutinated but not dissolved, although it can be shown that substances from the venom (intermediary bodies) have entered into combination with the corpuscles. If now a little fresh serum which contains the complement and by itself may be an excellent preservative of normal corpuscles, be added to these venomized corpuscles, they are promptly dissolved.

Preston Kyes, working in Professor Ehrlich's laboratory, in an investigation just published<sup>15</sup> on the mode of action of cobra venom, confirms the conclusion of Flexner and Noguchi concerning the amboceptor nature of cobra venom, and adds much that is new and important to our knowledge of this subject. He finds that the washed blood corpuscles of certain animals are directly dissolved by cobra venom, while those of other animal species require the subsequent addition of complements or adjuvants to bring them under the influence of the venom. But even in the former case a complementary body is essential to the reaction, this, however, being not a serum complement but an endocomplement contained within the red corpuscles. Of great significance is the demonstration by Kyes of still a third substance, namely lecithin, which is capable through combination with the venom intermediary body of completing the hæmolytic potency of venom.<sup>16</sup> The discovery for the first time of a definite, crystallizable substance with the power of uniting, like a complement, with an intermediary body and thus completing the formation of a cytotoxin is evidently of fundamental importance. The suggestion by Ehrlich and Kyes that possibly the cholin group is the toxophore group of lecithin is particularly interesting in the light of F. W.

<sup>14</sup> Preston Kyes: Ueber die Wirkungsweise des Cobragiftes. Berliner klin. Wochenschr., 1902, Nos. 38 and 39. I am greatly indebted to my friend Professor Ehrlich and to my former pupil Dr. Kyes in putting me in possession of the main results of these interesting experiments before their publication.

<sup>15</sup> The objections made by Calmette (Compt. rend. Acad. d. Sc., 1902, T. 134, No. 24) to Flexner and Noguchi's interpretation of their experiments as to the amboceptor nature of venom have been completely overthrown by the experiments of Preston Kyes.

<sup>16</sup> Flexner and Noguchi: Snake venom in relation to hæmolysis, bacteriolysis and toxicity. Journal of Experimental Medicine, March 17, 1902, Vol. VI, p. 277.

Mott's valuable studies of chemical processes concerned in degenerations of the nervous system.

The researches of Flexner and Noguchi and of Kyes therefore have taught us that in poisoning by venom the bodies of human beings and of animals contain in the form of complements, or alexins" as they are also called, the substances which are most directly concerned in the act of poisoning. The venom brings into the necessary relations with constituents of the body cells poisons we already harbor or may generate but which are harmless without the intervention of intermediary bodies. These poisons within us are powerful weapons, which, when seized by hostile hands, may be turned with deadly effect against our own cells, but which are also our main defense against parasitic invaders.

Flexner and Noguchi have demonstrated experimentally that, like the hæmolytic, so also the leukotoxic, the neurotoxic, and other cytotoxic properties of venom depend upon combinations of venom intermediary bodies with complements contained in the cells poisoned by venom or in the fluids bathing these cells. Particularly striking are their experiments showing in vitro and under the microscope the cytolytic action of cobra venom upon certain large molluscan nerve cells in the fresh state. The complement essential to this reaction is contained within the nerve cells. In previous experiments of Flexner and Noguchi there had been indications that intracellular complements are concerned in some of the toxic effects of venom upon cells. The positive demonstration by Preston Kyes of a special class of intracellular complements or endocomplements is unquestionably of great pathological interest, and seems destined to play an important part in the explanation of many morbid conditions in connection with endogenic and exogenic intoxications, probably also in such phenomena as self-digestion or autolysis.

Snake venom is a rich mine of diverse toxins, and, on account of its pathological importance, I must mention one of the cytotoxins discovered there by Flexner and Noguchi, as it may be that a similar toxin is produced by certain bacteria and under still other conditions. As is well known, one of the most striking lesions resulting from poisoning by certain venoms is the occurrence of abundant hæmorrhages in various tissues of the body. This effect has been generally attributed to the direct action of venom on the red corpuscles and on the coagulability of the blood, but the experiments of Flexner and Noguchi indicate that these hæmorrhages are due to the presence in venom of a cytotoxin which has the power of dissolving endothelial cells, in other words an endotheliolysin. Dr. Flexner suggests the name "hæmorrhagin" for this special toxin which causes extravasations of blood through its direct solvent action upon capillary endothelium, an effect which is readily demon-

strable under the microscope. It is hardly necessary for me to stop to emphasize the clinical and pathological importance of the discovery of an endotheliotoxin, a kind of poison which may prove to be of special significance in the interesting group of hæmorrhagic infections and perhaps also in purpura and kindred affections.

The foregoing newly discovered facts, which I have sketched only in bare outline, illustrate in a striking way the fruitfulness of methods and conceptions which we owe to recent studies of immunity. The results of these investigations, however, are significant beyond the mere facts disclosed, important as these are. They have for the first time revealed in normal toxic secretions, readily introduced under conditions of nature into the tissues of man and animals, cellular poisons akin to the complex hæmolysins, neurotoxins and other cytotoxins of immune and some normal sera, which have aroused so much interest and experimental study during the past four years. The most noticeable difference between the venom cytotoxins and those hitherto observed in immune sera is the far greater resistance to heat of the intermediary bodies of the former, but we are already acquainted with considerable variations in the sensitiveness to heat both of different intermediary bodies and of complements. That snake venom should contain only one-half of the complete poison, the other and the really destructive half being widely distributed in the blood and cells of man and of animals, is an instance of a curious kind of adaptation, of interest from evolutionary as well as from other points of view.

In consideration of the often emphasized analogies between venom toxins and bacterial toxins, these facts render it highly desirable to make a systematic search of bacterial cultures by proper methods and under suitable conditions for complex cytotoxins. At present substances of this nature are not known to exist in our cultures. There have been discovered, however, within the past three or four years certain bacterial toxins which have a curious resemblance in some of their properties to the complex antibodies of blood, although, so far as they have been carefully studied, they appear to have the simpler constitution of the soluble toxins, like those of diphtheria and of tetanus. I refer to the bacterial hæmolysins, leukolysins, hæmagglutinins, precipitins and coagulins. There is no reason to suppose that this list exhausts the number of those actually present, for it is evident that it includes chiefly bodies readily demonstrable in test-tube experiments. It would be surprising if cytotoxins which act specifically upon red and white blood corpuscles were the only ones of this class produced by bacteria; in fact we have every reason from pathological observations to believe the contrary.

It has become evident that more refined methods than mere observation of the coarse effects of injecting into animals the filtrates or the killed bacteria of our cultures are required for the detection of the subtler and more specific cellular poisons. Instances are rapidly increasing in which

"There is some objection to the use of the term "alexin" as a synonym for "complement," as the former was applied originally by Buchner to substances which we now know to be combinations of complements with intermediary bodies.

by improved methods cultures of bacterial species once believed to be practically devoid of toxicity are found after all not to be so poor in toxins, even of the soluble variety. One of the earliest and most instructive illustrations of this is the discovery by Van De Velde of a leukocyte-destroying poison, named leukocidin, in exudates caused by infection with *Staphylococcus aureus* and also in filtrates of staphylococcus cultures, which had been previously regarded as almost entirely free of toxic power.

More widely distributed in cultures of different species of bacteria are the hæmolysins, of which the first example, discovered in 1898 by Ehrlich in cultures of the tetanus bacillus, was carefully studied by Madsen the following year, and which have since been investigated by Kraus with Clairmont and with Ludwig, Bulloch and Hunter, Neisser and Wechsberg, Todd, Besredka, and others. The list of bacterial species known to produce in cultures substances of this nature capable of dissolving red blood corpuscles is already a long one and includes the bacilli of tetanus, of green pus, of typhoid fever, of acute dysentery, of diphtheria, of plague, the pyogenic staphylococci and streptococci, the pneumococcus and many other bacteria. Nuttall and I noted in our first description of *Bacillus aerogenes capsulatus* over ten years ago its capacity of laking blood so that I was not surprised to find recently that an hæmolysin can be demonstrated in cultures of this organism. The blood-destroying property appears to stand in no definite relation to virulence, nor is it limited to pathogenic bacteria. It pertains also to many putrefactive bacteria. The strongest bacterial hæmolysin hitherto observed was found by Todd in cultures of *Bacillus megatherium*, which is a widely distributed saprophyte.

As already stated, none of these bodies has been shown to belong to the class of complex hæmolysins in blood, which have been far more exhaustively investigated than any other of the specific anti-bodies. Doubtless there is at present among bacteriologists too great a tendency to attribute to the less carefully studied anti-bodies characters which have been worked out in detail only for the hæmolysins of immune serum. It would lead too far to attempt here a discussion of the special characters of the various bacterial hæmolysins, which present in different specimens curious and at present unexplained divergencies as regards resistance to heat and several other properties. It must suffice to indicate briefly what is known of the pathological importance of this interesting group of bacterial toxins.

In view of the abundant clinical and pathological evidence of extensive destruction of red corpuscles in the course of many infectious diseases, it is certainly significant to find that many bacteria are endowed with a specific hæmolytic power. The question is how far we are justified in applying to the actual conditions of infection the existing experimental data upon this subject. Assuredly here, as everywhere, results of test-tube experiments, helpful in suggestion as they may be, should not be utilized without further

evidence to explain morbid phenomena within the infected human or animal body. While much more work upon this subject is needed before our information will be exact or complete, the observations and experiments of Besredka,<sup>18</sup> Kraus and Ludwig<sup>19</sup> and others have already demonstrated that bacteria may exert their blood-destroying power within the living body. This hæmolytic capacity of microorganisms affords an explanation, although certainly not the only one, of the secondary anæmias which are such a marked feature of many infectious diseases, as streptococcic and other septicæmias, pneumonia, typhoid fever, scarlatina and others. The hæmoglobinuria which is a recognized, although rare complication of various infectious diseases, may be referable to intoxication with unusually powerful parasitic hæmolysins, or to an exceptional lack of resistance of red corpuscles. Hæmoglobin, however, is not necessarily present in solution in the blood-plasma, for the destruction of the damaged red corpuscles may take place within the large phagocytes of the spleen and the hæmo-lymph glands, as is well known to occur on an extensive scale in typhoid fever and some other infections. A familiar example of the action of bacterial hæmolysins is the post-mortem reddening of the inner lining of the heart and blood vessels, an effect which may be due to putrefactive bacteria or may appear very soon after death, especially from septicæmia caused by *Streptococcus pyogenes*, which, as has been shown, may lake the blood during life.

The fact that certain common saprophytic bacteria may produce energetic hæmolysins, as pointed out by Kraus and Clairmont and by Todd, has a possible bearing upon the etiology of certain obscure anæmias not of infectious origin, particularly upon the interesting observations and the theory of William Hunter concerning their causation by absorption of toxins from the alimentary tract. Todd found cultures of *Bacillus megatherium* so strongly hæmolytic that the intravenous injection of 1 cc. of the filtrate into guinea-pigs was followed by hæmoglobinuria, 10 cc. being fatal. Human red corpuscles are sensitive to this hæmolysin.

Normal human and other blood-sera contain in varying amounts anti-hæmolysins, which protect the red corpuscles from the action of some of the bacterial hæmolytic agents. Specific anti-hæmolysins are readily produced by immunizing injections of bacterial hæmolysins and are generated also in the course of infections. Lang suggests that the augmentation of the osmotic resistance of the erythrocytes which has been noted in some infectious diseases, as well as in icterus and some other morbid conditions, may be a reactive phenomenon caused by the presence of hæmolytic toxins.

Intimately associated with the hæmolysins in cultures are the bacterial hæmagglutinins (Kraus and Ludwig),<sup>20</sup> substances which have the power to clump red blood corpuscles. Among unicellular organisms both the capacity to produce agglutinins and the aptitude for agglutination seem to be

<sup>18</sup> Besredka: Annales de l'Institut Pasteur, 1901, XV, p. 880.

<sup>19</sup> Kraus and Ludwig: Wiener. klin. Wochenschr., 1902, p. 382.

<sup>20</sup> Kraus and Ludwig: Wiener. klin. Wochenschr., 1902, p. 120.

very widely distributed. The bacterial hæmagglutinins, in analogy with the bacterial hæmolysins, are apparently of simpler constitution than the serum agglutinins, being destroyed at 58° C., whereas the latter are not injured by temperatures under 70° C. In order to demonstrate in cultures the hæmagglutinins it is generally necessary to eliminate in some way the action of the associated hæmolysins, which can be done by using small quantities of the culture fluid or by keeping the mixture of fluid and red corpuscles at zero temperature.

I know of no observations directly demonstrative of the action of bacterial hæmagglutinins within the living body in infections, but this subject is of such recent knowledge that it has been as yet scarcely investigated. Certainly there are morbid conditions which seem highly indicative of the operation of substances agglutinative of red corpuscles. Probably everyone with large experience in the examination of fresh blood in disease has noticed that sometimes red corpuscles, examined immediately after withdrawal of the blood, have a peculiar tendency to form clumps which cannot readily be broken up. This phenomenon, which is certainly suggestive of the action of an agglutinating agent, I have observed especially in some cases of septic infections and of cirrhosis of the liver.

Furthermore I would emphasize the support given by the recognition of hæmagglutinins to views advocated many years ago by Hueter and by Klebs concerning the occurrence of thrombi composed of coalesced red blood corpuscles. Such thrombi I believe to be not uncommon in typhoid fever and other infections, especially in small blood-vessels. I have elsewhere called attention to the evidence in favor of the interpretation of many of the hyaline thrombi as derived from agglutinated red corpuscles.

It can scarcely be doubted that substances agglutinative of white blood corpuscles are also produced by certain bacteria and that these are concerned in the clumping of pus cells and of leukocytes within the living body, but it would not be profitable to discuss this matter without more exact information than we now possess.

In this connection I may say that not only the discovery of the bacterial hæmagglutinins but also that of the hæmolysins and the leukolysins is likely to shed new light upon certain aspects of the difficult subject of thrombosis. The red corpuscles undergo various morphological changes under the influence of different bacterial hæmolysins acting with varying intensity. Distortions of shape, throwing out of projections, and detachment of colorless particles resembling platelets can sometimes be seen. These observations are of especial interest with reference to the doctrine, already strongly supported, that platelet thrombi originate from disintegrated red corpuscles. Levaditi, and Neisser and Wechsberg have described, as the result of intravenous injections of *Staphylococcus aureus*, areas of coagulative necrosis in the rabbit's kidney, which they attribute to thrombi composed

of disintegrated leukocytes caused by the staphylococcus leukocidin, to which I have already referred.

I have dwelt at some length, although of necessity incompletely, upon the bacterial hæmolysins, leukocidins and hæmagglutinins, because we are better informed about these agents than concerning other members of this recently recognized class of bacterial toxins. I have already expressed the opinion that similar poisons acting specifically upon other cells of the body are produced by bacteria; indeed neurotoxins and nephrotoxins of this type have been reported. The difficulties in the way of direct proof of the existence of these other bacterial cytotoxins are greater than in the case of those acting upon the red and the white blood corpuscles, but doubtless they can be overcome. Of course we have evidence of the action of bacterial poisons upon various body cells, but this is not enough. At present we can apply only in a vague and unsatisfactory way to the explanation of pathological processes most of the knowledge of this kind which we possess. What is urgently needed is a separation of these poisons and a determination of their source, constitution, mode of action, and degree of specificity along such lines as have been followed so fruitfully in the investigation of the soluble diphtheria and tetanus toxins, those other toxins of bacteria and of venom already considered, and the cytotoxins of normal and of immune serum. The path leading apparently in the right direction has already been opened and, if I mistake not, its further pursuit is most promising of valuable results in the near future.

Consider by way of illustration how helpless we now are in our efforts to explain the characteristic lesions of typhoid fever on the basis of our knowledge of the properties of the typhoid bacillus. That these lesions are referable to the action of toxins cannot, I think, be seriously questioned. Especially from the investigations of Mallory we know that the most characteristic histological changes of this disease consist in the proliferation of the reticular or so-called endothelial cells of the lymphatic tissue of the intestine and the mesenteric glands and of similar cells in the splenic pulp, and in the assumption by these proliferated cells of remarkable phagocytic activities toward the lymphocytes in the former situations and toward the red corpuscles in the spleen. Mallory believes that these changes are best interpreted by supposing that the typhoid toxin directly stimulates to proliferation the endothelial cells, which then devour their offspring, the lymphocytes, and the red corpuscles. I have suggested as another explanation that the typhoid bacillus produces a lymphocytotoxin and an hæmolysin, and that the proliferation of the fixed cells is partly compensatory and partly for the increased production of macrophages. We already know that this bacillus generates a hæmolytic agent, and we also know that one of the effects of injection of hæmolysins is to increase greatly the number of macrophages containing red corpuscles in the spleen.

Through the kindness of Professor Flexner I have had the opportunity of studying the extraordinary changes produced

in all the lymphatic glands and in the bone marrow of rabbits by injections of lymphotoxic or myelotoxic serum obtained by treating a goose with lymphatic or marrow tissue of the rabbit. One of the most striking effects of this poison for lymphocytes and other leukocytes is the very extensive proliferation of the reticulum cells in the lymphatic nodes and of the marrow cells. In the light of these observations it is clear that a positive demonstration of the production of a lymphotoxin by the typhoid bacillus would materially advance our understanding of the morbid anatomy of typhoid fever.

Another lesion of this disease only second in importance to those mentioned is the occurrence of plugging of the small vessels. Dr. Fisher in my laboratory has recently shown that such thromboses are produced by the experimental inoculation of rabbits with the typhoid bacillus. I have already pointed out that many of these plugs are agglutinative thrombi.

Of course infectious diseases other than typhoid fever could also be cited, did time permit, as equally forcible illustrations of the aid which pathology may reasonably expect from more precise knowledge of the bacterial cellular poisons. It is probable that such knowledge will lead to improvements in the quality for therapeutical purposes of the so-called bacteriolytic sera, some of which, as now prepared, are not so wholly devoid of antitoxic properties as is often represented. We may also anticipate from investigations of the character indicated much light upon one of the most puzzling of bacteriological problems, the localization of bacteria in disease. Toxic lesions and the plugging of small blood-vessels are certainly often of decisive influence in determining this localization, as has been demonstrated especially for the staphylococcus pyæmias by Muscatello and Ottaviano.<sup>21</sup>

The toxins to which I have chiefly directed your attention in this lecture are those produced by bacteria. But, as already pointed out, we now know that the animal body has the power to produce specific poisons directed not only against invading bacterial cells but also against all sorts of foreign cells. Following the discovery by Belfanti and Carbone in 1898 of this capacity in relation to injections of blood a wholly new domain of biology has been opened to experimental research. Attention has been withdrawn for the moment to a considerable extent from the bacterial toxins and concentrated upon the animal cytotoxins. Here new facts and conceptions of absorbing interest have been disclosed in an abundance and with a rapidity which are simply bewildering.

It was my original design to include in this lecture a consideration in some detail of these animal cytotoxins but so much time has been occupied with other aspects of the subject that I am compelled to abandon this intention. This is perhaps less to be regretted inasmuch as I understand the main purpose of these lectures to be the presentation of

applications to medicine and surgery of scientific discovery, and it is precisely this side of the recent work on animal cytotoxins which seems to me in the main not yet ripe for profitable discussion on this occasion. It is true that facts of much scientific and practical interest have been discovered by the investigations, initiated by Shattock and by Grünbaum, followed by Landsteiner, Ascoli, Eisenberg, Kraus and Ludwig, and others concerning the isoagglutinative and isolytic properties of human sera in health and in disease. But the really great practical questions in this domain relate to the production of autocytoxicins in the human and the animal body. What is the nature of that very efficient regulatory mechanism underlying the horror autotoxicus (Ehrlich) which prevents either the action or the formation of autocytoxicins in consequence of absorption of our own degenerated and dead cells? Can this protective mechanism be overthrown by pathological states and self-generated cellular poisons become operative in the causation of anæmias, hæmoglobinurias, chronic interstitial inflammations, uræmia, eclampsia, epilepsy, and other diseases? To these and similar important questions the existing experimental data seem to me too insufficient and inconclusive to furnish any decisive answer at present. I share, however, the hope and belief of many that here is a field for exploration which, although surrounded with many difficulties, gives promise of discoveries of a far-reaching and important nature. I anticipate that some future Huxley lecturer will find in this realm a fascinating theme.

In this connection may be mentioned the great pathological interest pertaining to the recent investigations of Jacoby, Conradi and others on the phenomena of self-digestion or autolysis of inflammatory exudates and necrotic material within the living body. One can readily convince himself of the energetic action of autolytic ferments by the simple experiment of placing a piece of fresh pneumonic lung in the stage of gray hepatization under chloroform and noting the rapid solution of the exudate, in contrast with the absence of this process in earlier stages of the disease. Conradi finds that bactericidal substances, to which he attaches much importance, are produced in tissues and cellular exudates undergoing autolysis.

Although my theme relates especially to the bearing of studies of immunity on pathology, it is hardly necessary to say that these studies were primarily undertaken to elucidate the great problems of predisposition and of resistance to disease and that in this field they have borne their richest fruits. It is especially gratifying to note the close convergence of the two doctrines of immunity, the cellular and the humoral, brought about by these recent discoveries. On the one hand the phagocytic school, represented so brilliantly by Metchnikoff and his co-workers in the Pasteur Institute, recognize and apply to the fullest extent in the explanation of acquired immunity the cytolytic principles based upon the cooperative action of intermediary bodies and complements. On the other hand the humoral school,

<sup>21</sup> Muscatello and Ottaviano: Virchow's Archiv, 1901, CLXVI, p. 212.

led by our German confrères, which has been so fruitful in results of the greatest scientific and practical value, recognize the cells as the immediate source of the protective substances. There are many differences in details, especially in terminology and in interpretation, which make the divergence seem greater than it really is. The essential difference between the two schools concerns the place where the two forces, intermediary body and complement, unite. All are agreed that the intermediary body exists free in the blood-plasma, but Metchnikoff strenuously insists, especially on the basis of Gengou's experiments, that the complement or cytase is within the leucocytes, from which it is not secreted but can be liberated only through damage to these cells. This question certainly needs further investigation before it can be regarded as settled. The recent recognition of endocomplements through researches made in Ehrlich's laboratory marks a still closer approximation of the two schools.

The deeper insight which we have recently gained into the nature of the forces concerned in immunity makes especially desirable the systematic study of the blood and other fluids of human beings in health and in disease with reference to their content of specific anti-bodies, particularly of the bactericidal substances. It can scarcely be doubted that knowledge of this kind will be in various ways of practical value to the physician and surgeon. The simplest procedure and the one hitherto generally adopted is the estimation of the bactericidal power of the blood-serum in toto. For this purpose Professor Wright<sup>22</sup> has devised an ingenious method, which in his hands has furnished extremely interesting information concerning variations in the bactericidal power of the blood as regards the typhoid bacillus in health, under the influence of fatigue, in the course of typhoid fever and after anti-typhoid inoculations. The older methods, however, while not without value, do not inform us of the total content of the blood in immunizing substances, and have led to very discordant results, particularly as to the influence of infection upon the bactericidal power. Thus Conradi<sup>23</sup> finds, in opposition to most previous experimenters as well as to the later results of Wilde, that infection with the anthrax bacillus does not at any stage influence materially the bactericidal properties of the blood.

A useful and readily applicable method for the determination separately of the intermediary bodies and of the complements of human serum is urgently needed. When one takes into consideration the plurality of complements and of intermediary bodies, the fallacies of interpretation which may arise from failure to take account of anti-complements, of anti-immune bodies, of complementoids, of amoceptoids, of deviation (Ablenkung) of complements, and

other principles in this complicated subject it is clear that the problem is not an easy one.

Notwithstanding these difficulties work has already begun along these new lines and has led to interesting results. We know that the content of the blood in specific anti-bodies, and especially in complements, varies in significant ways under diverse conditions, as in infancy and in adult life, in health, in different states of nutrition, under the influence of fatigue, of inanition, of pain, of interference with respiration, of alcohol, and in disease. The infant comes into the world with protective anti-bodies in its blood smaller in amount and less energetic than those possessed by the healthy adult. It is an important function of the mother to transfer to the suckling through her milk immunizing bodies, and the infant's stomach has the capacity, which is afterward lost, of absorbing these substances in an active state. The relative richness of the suckling's blood in protective anti-bodies, as contrasted with the artificially fed infant, explains the greater freedom of the former from infectious diseases.

The important question of the influence of pre-existent disease in predisposing to infection has been brought nearer to a solution by recent studies of immunity. Schütze and Scheller<sup>24</sup> have demonstrated that while the normal rabbit promptly regenerates the complements used up in consequence of the injection of hæmolytic serum, a rabbit infected with the hog-cholera bacillus has lost this capacity. My former pupil, Dr. Longcope, has kindly placed at my disposal the unpublished results of an investigation which he is making under Professor Flexner's direction at the Pennsylvania Hospital of the intermediary bodies and the complements in human blood in different diseases. Colon and typhoid bacilli are used as the tests, as, unless one accepts Bordet's doctrine of the unity of complements, it is more important for the study of problems of infection to determine bacteriolytic rather than hæmolytic anti-bodies. One of the earliest results of the systematic bacteriological examinations which we make at all autopsies at the Johns Hopkins Hospital was the recognition of the great frequency of terminal infections, formerly often undetected by the clinician, in chronic diseases, particularly of the heart, the blood-vessels, and the kidneys.<sup>25</sup> Dr. Longcope finds, although not regularly, still in many cases of these diseases a marked reduction in the quantity of complements, which may amount to a total loss of the colon complements. The analysis of the cases brings out unmistakably a definite relation between this loss of complement and the predisposition to infections.

The study of a series of acute infections, chiefly of a surgical nature, shows that in the course of the infection complements are being constantly used up and regenerated,

<sup>22</sup> A. E. Wright: *Lancet*, 1898, I, p. 95; 1900, II, p. 1556; 1901, I, pp. 609 and 1532; and 1901, II, p. 715.

<sup>23</sup> Conradi: *Zeitschrift für Hygiene*, 1900, XXXIV, p. 185; 1901, XXXVIII, p. 411.

<sup>24</sup> Schütze and Scheller: *Zeitschr. f. Hygiene*, 1901, XXXVI, pp. 270 and 459.

<sup>25</sup> Flexner. A statistical and experimental study of terminal infections. *Journal of Experimental Medicine*, 1896, Vol. I, p. 559.

and that at any given time there may be an excess or a reduction of the bactericidal power of the blood. Thus far it has been found impossible in these acute infections to attach any prognostic significance to the amount of complement or of bactericidal power. Hyperleucocytosis was often, although not invariably, associated with high content of complements for the bacteria tested.

Although we have traversed, gentlemen, in this lecture a path which I fear has seemed to you a long and winding one, I am conscious that I have been able to point out the features of the prospect only imperfectly and incompletely. The extent and the richness in details have been embarrassing. I trust, however, that I have been able to indicate in some measure the great interest and importance to biology, to physiology, to pathology, to every department of medical science and art of investigations which have led to a deeper insight into certain manifestations of cellular life. What has been conquered by these investigations is simply a bit of new territory pertaining to the intimate life of the cells, and we find here, as whenever we are able to penetrate deeper into this life, that there comes a flood of new light into

every department of biology. The researches on immunity, which to some of short vision once seemed to threaten the foundations of cellular pathology, have served only to strengthen them. These researches, which have already led to the saving of thousands of human lives and will lead to the saving of untold thousands more, have been carried on by the experimental method and can be conducted in no other way. This method is as essential for the advancement of medical science as for that of any of the natural or physical sciences. To restrict unnecessarily and unjustifiably its use is nothing short of a crime against humanity. It is an evidence of the robust vitality of English physiology and medicine that in spite of unwarrantable obstacles thrown in their path their contributions to science in recent years have been so numerous and so important. The influence of English thought and action is great with us in America. See to it, my colleagues and men of science in these British Isles, that you retain for yourselves and hand down to your successors, at least without further impairment, the means of promoting medical knowledge and thus of benefiting mankind.

## THE IMPORTANCE OF A MORE RADICAL OPERATION IN CARCINOMA CERVICIS UTERI AS SUGGESTED BY PATHOLOGICAL FINDINGS IN THE PARAMETRIUM.

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No wonder that the laity and even some physicians consider cancer of the cervix of the uterus an incurable disease, for three-fifths of the patients admitted to this hospital with cancer of the cervix come too late for anything but palliative treatment. Of 143 patients in which hysterectomy has been done, 21 cases have died as a result of the operation, giving a primary mortality of 14.6 per cent. Three years or more have elapsed since the operation in 69 cases which we have been able to follow, and at the end of that time 20 were living, but 6 of these later had recurrences, thus giving a percentage of recurrences after three years and more, of 79.7 per cent. When we consider those cases in which five years or longer have elapsed since operation we find that there have been 49 whom we have been able to follow, and of this number the growth returned in 43, or 87.7 per cent. We realize, however, that five years is not long enough, for 2 of our patients have died at the end of 6 and 7 years from general carcinosis without a return in the vaginal vault, and a third is living, with a small growth in the vaginal scar, five and a half years after operation, there having been symptoms referable to it for only two months.

The comparison of statistics is very unsatisfactory, for many will operate on favorable cases only and will include in their statistics those cases alone in which they

think that the entire growth has been removed; while others (as has occurred in many instances in our operating room), have realized before the operation that the growth was probably inoperable and at the close of the operation have felt sure that the entire growth had not been removed. Generally the unfavorable prognosis has been speedily confirmed; on the other hand, we have had the satisfaction of seeing a few cases which are apparently well two and three years after operation, but which were considered unfavorable even at the close of the operation. Wertheim has emphasized that the induration of the broad ligament may be inflammatory and not cancerous in origin, and as we know, enlarged lymph glands do not necessarily indicate carcinoma. It is consequently impossible to make a positive prognosis before an operation or even at the close of one. We have every reason to expect, and even promise, a much higher percentage of cures in the future, for great advances have been made in recent years in two directions:

First, not only the medical profession, but also the laity, realize the importance of making an *early* diagnosis.

Second, the operation is *more radical*, not only in advanced cases but also in *favorable ones*.

The importance of removing the lymph glands along the pelvic vessels has been emphasized by many operators and

credit is due especially to Wertheim,<sup>11</sup> who has reported 3 series of cases operated upon by his method. In 30 of the 90 cases reported by him, there was evidence of glandular metastases, as determined by serial sections of the glands. He advocates not only dissecting out the glands but also a wide excision of the parametrium and vagina. While he thinks it is better always to remove the glands, he has found carcinoma only in the enlarged glands, consequently he has removed them in only 22 of the 30 cases last reported by him, and in 11 of these cases carcinoma was found. He has shown that there is no relation between the size of the primary growth and the presence or extent of glandular involvement; i. e., the local growth may be very small and yet there may be extensive glandular involvement. On the other hand, the primary growth may be large and there may be very few or no metastases to the lymphatic glands.

Doederlein<sup>12</sup> reports 26 cases operated upon by Wertheim's method. In 18 the glands were removed and in 7 of these carcinoma was found. In 1895 Ries,<sup>13</sup> Rumpf<sup>14</sup> and Clark<sup>15</sup> advocated that the lymph glands should be removed in hysterectomy for cancer of the uterus. Their operations are apparently similar. Ries,<sup>13</sup> in a paper read before the Illinois State Medical Society, May, 1901, emphasizes the importance of this procedure and calls attention to the necessity of serial sections in order to prove the existence of carcinoma in the glands, and that one cannot tell by palpation whether or not the gland contains carcinoma, for a large, firm gland may be normal and a small, soft one may contain metastases. Clark,<sup>15</sup> in an article which appeared, May, 1901, states, "As a result of my own study of glands which have been removed at the time of radical operation for cancer, I have gradually reached the conclusion that glandular metastases are much less frequent than I supposed when I originally described my own operation in 1895. Recently I have become more and more conservative as to my statements on this point, for the result of Cullen's very careful investigation of all cancer cases operated on in the Johns Hopkins Hospital proved that metastases are comparatively infrequent." He then considers the work of Wertheim, who emphasizes the importance of serial sections, and adds that "if this be true we may be wrong in assuming that metastases are not frequent." In speaking of the operation, he says, "Notwithstanding my conviction as to the necessity for the removal of the glands, I believe that the condition of the patient must be considered carefully before proceeding to this step. My rule is, therefore, to complete first the chief part of the operation, the removal of the uterus, and if then the patient's general condition justifies it, the iliac glands may be dissected out. Even then, I consider the removal of the glands of prognostic rather than curative value, for if they are involved as shown by microscopic examination, I do not believe the patient will escape a recurrence of the cancer." Wertheim, in the report of his last series of 30 cases, refers to patients who were operated upon 2, 2½ and 3 years ago, where cancerous glands were removed, and as yet there is no evidence

of a recurrence. The results of the work in this hospital in regard to the involvement of the lymph glands is of little value when negative, for they have not been systematically removed and serial sections have been made in only a few instances.

Associated with these 143 cases of hysterectomy for cancer of the cervix in this hospital there have been 17 instances of unintentional injury to the ureter. The more radical the operation and the greater the endeavor to get well outside of the growth, the more liability there is to be an injury to the ureter. These injuries have been of various kinds, as clamping, ligating, and incising the ureter. Some were recognized during the operation and the ureter was released or repaired; in others, the injury was not discovered until afterwards. In 7 instances, post-operative uretero-vaginal fistula occurred from injuring the blood supply of the ureter. The main blood vessels of the ureter are in its outer loose fibrous coat. When the ureter is adherent to the growth, dissecting it free will injure these vessels, as will also clamping it; and the injury may be sufficient to give rise to a slough and a resulting urinary sinus. From our experience it would seem that when there is lateral extension of the disease sufficient to cause the ureter or ureters to become adherent, it is better to remove all the tissue between the growth and the pelvic wall, thus including the vesical portion of the ureter and implant the end of the ureter in the bladder. The points in favor of this procedure are that—

1. The growth is less likely to return.
2. Uretero-vaginal fistulae are probably less likely to occur.
3. The time spent in doing it is probably no greater than would be required to dissect the ureter free.

In July of this year I had an opportunity to operate on a case of cancer of the cervix in which clinically there was some induration of the right broad ligament. I therefore planned to sacrifice the right ureter and implant it in the bladder. Previous to the operation I reviewed the operations of Clark, Wertheim and others, and at the same time worked out a form of uretero-vesical implantation, which I tried with success in dogs. From the above considerations and a study of the anatomy of the pelvis I developed the various steps of an operation which I first tried upon the cadaver. Since then three carcinomatous uteri have been removed by this operation—the first by myself and the remaining two by Dr. Schenck, Resident Gynecologist. Another was attempted but abandoned on account of the very wide extension of the disease and the difficulty in obtaining a satisfactory exposure, due to the depth of the pelvis and very thick abdominal walls; the uterus and only a portion of the growth were removed. The operation which I am about to describe is in general the one we used, modified by the experience gained from these cases. In the first case the lower end of the right ureter was excised and in the second the left, which was double, and in the third both ureters.

## OPERATION.

1. A preliminary catheterization of the ureters, with silk bougies, before the patient takes the anesthetic. I failed in my case on account of the vesical irritability, but Dr. Schenck succeeded in his two cases and found them of great assistance.

2. After the patient is anesthetized she is placed in the perineal position and a long proctoscope is inserted through the rectum high up into the large intestine in order to get rid of any gas or fecal matter which may be present.

3. A row of interlocking catgut sutures is now placed around the vagina, 3 cm. below the growth. These sutures are passed with a large curved needle, include large masses of tissue, and extend laterally as far as the needle will permit, while a finger in the rectum prevents their being passed too deep posteriorly. After all these sutures have been passed they are tied. This procedure is for the purpose of occluding the large vaginal and paravaginal veins which give rise to the venous hemorrhage so troublesome and at times dangerous, when a wide lateral dissection of the growth is attempted from above. Dr. Miller, at one time resident gynecologist, introduced a very useful step in abdominal hysterectomy for cancer of the uterus. He placed sutures in the vaginal wall below the growth and with a Pacquelin cautery burned through the vaginal wall between the sutures and the growth. This was done preliminary to the abdominal operation and the groove caused by the cautery indicated how much of the vagina was to be removed, and the sutures were for the purpose of preventing bleeding from the vaginal wall. These sutures were passed with a small needle and probably only occluded veins in the vaginal wall. Profiting by his work, I go a step further, using as large a needle as the vagina will permit and passing the sutures as stated, but do not burn through the vagina, for the tying of these large masses of tissue constricts the vaginal canal so that the burning is not possible. The sutures should not be placed too near the cervix in the antero-lateral portion of the vagina, for there is danger of ligating the ureters, should the operator not wish to sacrifice them later.

4. A retention catheter is now placed in the bladder, so that the bladder may be filled with sterile fluid to help detect a hole in the bladder and also to aid in the uretero-vesical implantation.

5. The patient is now placed in the Trendelenburg position and the abdomen is opened from symphysis to umbilicus. A self-retaining retractor is used. After packing back the intestines with gauze, the ovary of the side on which the ureter is to be resected is grasped by a pair of forceps and pulled downwards and outwards, thus making taut the ovarian vessels and peritoneum covering the iliac vessels. The peritoneum is now split below and parallel to the ovarian vessels as high up as the origin of the internal iliac artery. The ureter can be seen in a thin patient lying in the lower peritoneal flap, and its blood supply is not interfered with. Beginning at the origin of the internal iliac artery we now

dissect downwards removing the fat and lymphatic structures, including glands from along the iliac vessels, thus exposing the branches and removing the tissue *en masse*. By using a blunt dissector and always dissecting down along the vessels, hemorrhage may be avoided. One should never dissect upwards for the following reasons:

(a) For then the instrument will enter the angle between the branches of the iliac vessels and may tear off one, and when a branch is torn in this manner from a larger one the hemorrhage comes from both vessels if they are veins, as they are very apt to be, or possibly from only the larger one, if it is an artery.

(b) By dissecting downwards the lymphatics and adipose tissue can be removed *en masse*.

(c) It is always much safer to work from a more dangerous to a less dangerous area, for when one works towards the large vessels, a slip of the instrument may give rise to serious hemorrhage.

After exposing the vessels in this manner down to the uterine artery, the ovarian vessels and round ligament are cut. The uterine artery is tied twice at its origin, taking care to include in the ligature the vaginal artery should it arise from the internal iliac, but not the superior vesical artery, and cut between the two ties. I do not think that there is anything to be gained by tying the anterior branch of the internal iliac, as was done in two of the cases, and there is the disadvantage that the blood supply of the pelvis may be injured.

6. The other side is treated in a similar manner, if both ureters are to be removed, as was done in one instance; if not, the exposure of the vessels is the same and the removal of the lymphatics may be the same and the uterine vessels are tied and cut at their origin, and then lifted up and dissected away from the ureter, taking care not to injure its outer vascular coat.

7. The uterus is now pulled upwards towards the umbilicus and the bladder is dissected free from the cervix and not the cervix from the bladder, for in the former, while there is greater danger of injuring the bladder, there is less danger of cutting into the diseased cervix. The dissection is carried on down to the ureters and, if thought best, one or both are cut off close to the bladder.

8. If the lower end of the ureter is to be sacrificed, it should be amputated just above the place where the uterine artery crosses it, and all the tissue lateral to the cervix including the lower portion of the excised ureter, may be dissected from the pelvic wall. If the lower end of the ureter is not to be sacrificed, the parametrium is dissected free mesial to the ureter.

9. The utero-sacral ligaments are next cut and the rectum is dissected from the cervix and vagina.

10. The dissection is now carried on around the growth on all sides and down the vagina to the preliminary catgut ligatures. The gaping openings of the large veins can be seen in these cases, some thrombosed and others empty, perfectly controlled by the preliminary catgut sutures. One

has to be careful not to go too far laterally below the growth, for here one may cut veins which come in from the sides and are not controlled by the preliminary sutures. Wertheim's clamps are now applied to the vagina and the vagina is cut below them and the tissue removed.

#### 11. The uretero-vesical implantation.

The table is placed in the horizontal position. The ureter is split laterally for a distance of 8 mm., so as to form a dorsal and a ventral flap. A silk suture with a needle at both ends is passed through each flap from side to side just beneath the ureteral mucosa. The bladder may be filled with sterile water or else the posterior wall may be pulled from the anterior wall by thumb forceps. Choose a place in the bladder with a good blood supply, make two parallel horizontal incisions, the width of the ureter apart and as wide as the same and connect these two by a transverse incision. This gives a  $\pi$  incision, and on spreading the flaps apart forms a square hole in the bladder with two lateral flaps. The needles are next passed through this hole and through the bladder wall from within out, those from the dorsal flap, coming out below the opening about 5 mm. from the edge and the width of the ureter apart, and those from the ventral flap coming out at corresponding places above the opening. The ureter is now drawn into the bladder by the sutures and they are tied. The lateral bladder flaps are now sewed to the side of the ureter with fine silk sutures which pass through ureteral and bladder wall down to the mucosa. The anastomosis is complete, except for the buttressing of some of the tissue about it. Its advantage is its simplicity. There is little chance for ureteral stricture on account of the square hole in the bladder; the implantation is strong, silk being used, two sutures of which pass through the entire bladder wall and ureteral wall except the ureteral mucosa, while the other two sutures include the ureteral and vesical muscular coats. All sutures are tied outside of the bladder, and are not exposed in the cavity of the bladder so as to form the nucleus for a stone. Nevertheless one should always make a cystoscopic examination before the patient is discharged to make sure that this has not occurred. The ureter and raw areas are now covered with peritoneum, the pelvis is drained through the vagina, and the abdomen is closed. The technique of covering the raw areas caused by abdominal hysterectomy for cancer of the cervix with special reference to the support of the bladder has been very carefully worked out by Krönig."

Such an operation at present takes from 2½ to 3 hours. The passing of the preliminary sutures in the vagina takes from ten to fifteen minutes, while the abdominal operation, including the uretero-vesical anastomosis, takes from 2 to 2½ hours. The uretero-vesical implantation can be done in ten minutes.

The advantages gained by sacrificing both ureters and removing the lymphatics along the pelvic vessels are well shown in Fig. 1, where all the tissue from pelvic wall to pelvic wall including the lower 4.5 cm. of the ureters was removed with the uterus and lymphatics along the pelvic

vessels. One by drawing an imaginary line between the ureters and the cervix can see the difference between removing all this tissue and simply doing a "hysterectomy" for cancer of the uterus. The comparison between the two operations is also shown in Fig. 2, which is a cross section of a case where the ureter was sacrificed on one side only.

These three operations gave excellent opportunity to study the conditions found in the parametrium between the cervix and the pelvic wall, including the ureter.

I give a brief summary of the points of interest in these cases:

Case No. 1. Gyn. No. 9802. Path. No. 6019.

Clinically the right parametrium seemed a little thicker than the left. Many sections were cut of this tissue; a few small lymph nodes, .5 to 1 mm. in diameter, were found along the blood vessels out as far as the ureter. Small groups of carcinoma cells were found in the lymph channels one-third of the distance from the cervix to the ureter. Somewhat similar conditions have been described by Cullen<sup>11</sup> and others. There was nothing in the section to account for the apparent increased density of the tissue. Had a vaginal hysterectomy been done, cancer would probably have been left behind.

There was no evidence of cancer found in the one lymph gland removed from the iliac vessels.

Case No. 11. Gyn. No. 9860. Path. No. 6074 (Figs. 2 and 3).

Clinically the left parametrium seemed thicker than the right.

Blocks were cut from the parametrium and serial sections were made. At the level of the uterine artery, scattered along it and some of the other vessels were found lymph nodes from 1 to 3 mm. in diameter. These may have accounted for the apparent increased density of the tissue. There was not any evidence of cancer in the lymph nodes at this level. In a block taken at a lower level a few small lymph nodes were found along the veins. The diameter of the largest was 1.5 mm. and the largest number found in any one section was 5 (see Fig. 3), while many sections contained only 1 or 2, and some sections none. Cancer metastases were found in these small nodes, and Fig. 3 was drawn from a section in which cancer was present in the node marked *d*, which is lateral and posterior to the double ureter. In other sections cancer was found in a node at about the same position as the nodes marked *c*. These were the only nodes found in the parametrium with cancer and they would not have been found unless serial sections had been made, for many sections may be made of one small node 1 mm. in diameter, and only 1 or 2 of these sections will show cancer. Cancer was not found in the lymph spaces as in No. 1. The lymph glands along the pelvic vessels on the left side were not removed, for they could not be palpated. On the other hand, an enlarged gland lateral to the right ureter showed carcinoma, and yet the right parametrium felt normal and consequently the right ureter was not sacrificed. Had the ureter been sacrificed, we would have had an opportunity to

study this tissue between the cervix and pelvic wall, and possibly we may have found these small lymph nodes with cancerous metastases, for certainly a few scattered lymph nodes 1 to 1.5 mm. in diameter cannot be felt in a mass of fibrous and adipose tissue.

Case No. III. Gyn. No. 9903. Path. No. 6103 (Fig. 1).

Clinically both ureters were adherent to or surrounded by the thickened parametrium. The growth had extended out to the ureters and it would have been impossible to remove the uterus and leave the ureters without injuring them and leaving the malignant growth behind, so it seemed that the lower ends of both ureters must be sacrificed or the operation abandoned. Therefore the lower ends of both ureters were removed with the uterus by Dr. Schenck.

In vaginal and likewise abdominal hysterectomies the separation of the uterus from the surrounding tissue takes place mesial to the ureter in tissue composed of fibrous and adipose tissue, blood vessels and lymphatics. We may very well speak of it as the axilla of the cervix. The cervix is hard and firm, this tissue is loose and easily torn, therefore the line of separation will naturally take place at the junction of the hard tissue and the loose, very near the cervix. Should there be any lateral extension of the disease into the lymphatics it will probably be left behind.

If it is an abdominal operation and the operator removes the enlarged lymph glands, the procedure seems to me to be analogous to that of a surgeon who excises a cancer of the breast, dissects out some enlarged lymph glands in the neck and leaves untouched the lymphatics in the axilla. Wertheim emphasizes the importance of a wide excision of the parametrium and vagina and a dissection of the pelvic lymph glands. He exposes the ureter and ties the uterine vessels just over it. The uterus is then removed with a wide excision of the parametrium and vagina. The lymphatics are now dissected from the pelvic vessels if the glands are enlarged; otherwise they are not removed. Can he by such an operation remove all the tissue from the cervix to the pelvic wall without interfering with the blood supply of the ureter or leaving cancer in the pelvis? Would such an operation remove a lymph nodule posterior and lateral to the ureter, as *d* in Fig. 3?

In regard to vaginal hysterectomy, it is impossible to remove lymphatic glands and we realize that they are involved in at least one-third of the operable cases, as shown by Wertheim. But then, he who advocates vaginal hysterectomy may say that when the lymphatics are involved the case is hopeless. This must be proven.

#### CONCLUSIONS.

1. Carcinoma of the cervix may metastasize to small lymph nodes along the blood vessels, and these nodes may have a diameter of not over 1 to 1.5 mm.

2. As the nodes are very small it may be impossible to feel them either in the parametrium or along the pelvic vessels.

3. These metastases may be so minute and scattered that

they can be discovered only accidentally or by cutting serial sections.

4. In every case of hysterectomy for carcinoma of the cervix the lymphatics along the pelvic vessels, and also the parametrium, should be removed *en masse* with the uterus, because an enlarged gland is not necessarily an invaded gland and cancer may be present in very small lymph nodes which can not be palpated; therefore clinically it is impossible always to diagnose cancerous lymphatics.

5. Should the ureter be adherent to the parametrium, the lower portion of it should be sacrificed and all the tissue from cervix to pelvic wall removed, for if the ureter is dissected free, two things are very apt to occur: (1) The disease will probably return. (2) An uretero-vaginal fistula will probably occur from injury to the blood supply of the ureter.

6. To the above should be added a last suggestion that in every case of hysterectomy for cancer of the cervix the lymphatics should be removed from the pelvic vessels from above downwards, together with the uterus and all the tissues lateral to the cervix from pelvic wall to pelvic wall undisturbed, including the lower 4 cm. of the ureters; and the ureters should be implanted in the bladder.

Wertheim has shown that the local disease may be very small, and yet the glands may be involved, and if the glands are involved probably the tissue between them and the cervix is also involved and the involvement may be in such small areas that it cannot be diagnosed clinically. So one would think that probably the *most radical operation* was indicated in the *most favorable cases* as much if not *more* than in the cases with extensive involvement, for in the former there is the greater chance of removing the entire growth.

These questions naturally arise: Is such an operation justifiable? What will the primary mortality be? What will be the percentage of cures? Is it necessary to sacrifice the lower end of the ureter, and why can it not be dissected free and the tissue all about it removed?

These answers all require time and work, and so far neither sufficient time has elapsed nor enough work has been done to confirm or condemn such a procedure. As stated, the operation with removal of one ureter has been done twice, with one death. In that instance the posterior iliac veins and rectum were accidentally injured and the patient died from shock with post-operative anuria. The complete operation with removal of the lower ends of both ureters has been done once, and that by Dr. Schenck, the ureters being adherent to the growth. In another case the operation was attempted, but abandoned on account of the wide extension of the disease and large size of the patient, making the exposure very difficult. What will be the ultimate fates of the two patients who are living remains to be seen.

In any operation there is the possibility of perfecting the various steps so that they may not only be done more quickly but also with less shock to the patient. A very good example of this is shown in the 90 cases reported by Wertheim. The duration of the operation in several cases in the first series reported by him was from 2 to 3 hours, the same

length of time that we have consumed in this operation, while in his last 30 cases the duration of the operation, including the closure of the abdomen, varied from 1 to 1½ hours, just one-half the time of the cases above referred to. In his first 30 cases there was a primary mortality of 12 cases; in the second 30, of 5; and in the last 30, only 3. And I am sure all physicians interested in cancer of the uterus are looking forward to find out what per cent of the cases surviving the operation are free from recurrence at the end of three and five years, and whether the recurrence is local or glandular, and especially what per cent of those in whom cancerous glands were removed are well at the end of these periods. For, as stated, Wertheim removes the uterus with as wide an excision of the parametrium as is possible without injuring the blood supply of the lower end of the ureter, as has been worked out by Feitel." The lymphatics are then removed from about the pelvic vessels. One would think that if the lymphatics about the pelvic vessels are cancerous, probably the tissue between them and the growth would also contain cancer, hence we could expect a return in these cases in the tissue about the ureter and lateral to it near the pelvic wall, which would have been removed had the lower end of the ureter been sacrificed as has been described.

The operation which I have described is more difficult than the one described by Wertheim, so we must expect that it will take longer, and we can hardly hope ever to be able to do it in 1 and 1½ hours, as Wertheim is able to do. Likewise, the operation will undoubtedly be attended with a higher primary mortality on account of the greater length of time consumed in doing it, the greater liability of post-operative infection due to the large cavity left in the pelvis by the removal of so much tissue, which fills in very slowly, and also to complications which may be associated with the uretero-vesical implantation. The hemorrhage from the vaginal and paravaginal veins, so dangerous in our previous operations, can apparently be controlled by preliminary vaginal sutures, and thus one great source of shock avoided.

All the steps in the operation are open to development and much improvement. I am sure that many of us who are only too well acquainted with the mental and physical torture, the pain, the vesical and rectal fistulæ, etc., so generally associated with the clinical course of cancer of the cervix not operated upon, and the fact that such a large per cent recur after operation, which means that they have not escaped the above mentioned misery, will agree that any operation, no matter how severe, which gives the highest percentage of cures is the one to be developed, not only in the advanced cases, but especially in the early ones, for, as stated, in the latter there is the greater chance for a cure. And such an operation is the removal of the primary growth with as wide an excision as possible, and *en masse* with it, the tissue *undisturbed*, containing the lymphatics draining the region of the growth. We all know what such an operation has done for cancer of the breast and also for cancer in other

portions of the body, and cancer of the cervix of the uterus is not an exception.

In closing, I wish to thank Dr. Kelly for permission to make this report and Mr. Max Broedel for assisting me in making the illustrations.

October 6, 1902.

#### ADDITIONAL REMARKS.

The difficulty of obtaining a satisfactory exposure in fleshy individuals, as well as the long time spent working in the peritoneal cavity, a great factor in the causation of shock, suggests the use of the retroperitoneal route. Through incisions lateral to the outer borders of each rectus or a curved cross abdominal incision, the peritoneum could be exposed and dissected free from the pelvic wall. Thus, the greater part of the operation could be done extraperitoneally; namely, the dissection of the lymphatics from the pelvic vessels, the control of the uterine artery, and freeing of the cervix and parametrium from the pelvic walls and bladder. The time spent working in the peritoneal cavity would be very little, thus diminishing both the shock of the operation and the chance for infection. Two methods of operating by the extraperitoneal route have already been described by Amann" and Mackenrodt."

A feature of much interest in the development of a more radical operation is the possibility of saving the ureters in the cases where the parametrium is apparently not involved by the carcinoma. The blood supply of the ureter varies greatly; two of its main vessels are derived from the renal and ovarian arteries and all along its course it may receive branches from the vessels nearest to it, as the aorta, iliacs, uterine and vesical arteries. Monari" has called attention to the fact that the vessels run in the outer perimuscular connective coat, and emphasizes the importance of the branches from the renal and ovarian arteries, for they may accompany the ureter almost to the bladder. He states, therefore, that the ureter may be freed for nearly its entire length without causing a slough. This statement of Monari has been confirmed clinically, for many operators have isolated the ureter for a distance of several centimeters and yet a slough has not taken place. Wertheim had 5 cases of post-operative ureteral fistulæ in his second series of 30 cases, and 3 of the 5 were double, making in all 8 fistulæ. He had been isolating the ureter for nearly its entire pelvic length. Feitel studied the blood supply of the pelvic portion of the ureter and showed that the upper part received branches from the aorta and iliac vessels and that these branches entered the ureter from the mesial side, while those supplying the lower portion were derived from the uterine and superior vesical arteries, thus coming in lateral to the ureter. As a result of Feitel's work, the ureter in the next series of 30 cases was exposed differently. The peritoneum over the upper pelvic portion of the ureter was split open lateral to it and then the incision crossed the ureter and was continued down mesial to it, and thus the blood supply was not interfered with. In this series of 30 cases there were only 2 ureteral fistulæ and they resulted

from dissecting free the ureters, which were adherent to the growth, thus injuring the perimuscular vascular coat. We can see that there is clinical evidence for believing that in some cases the renal and ovarian vessels are sufficient to supply the ureter for nearly its entire length. On the other hand, there is equally strong evidence to show that in other cases the blood supply from the pelvic vessels is apparently necessary for the nourishment of the lower portion of the ureter. If the lower end of the ureters is not sacrificed, we realize that the tissue containing the lymphatics which drain the cervix has not been removed undisturbed, also that possibly carcinomatous tissue has been left behind; and then again that the blood supply of the ureter may have been injured sufficiently to give rise to a fistula, due either to handling of the ureter, thus injuring its perimuscular vascular coat, or injuring directly the blood vessels supplying that portion of the ureter. After the exposure of the ureter, whether its outer perimuscular vascular sheath is injured or not, it should again be brought in contact with tissue upon which it usually rests and should be covered with peritoneum. A drain should extend to a place near the ureter but should never come in contact with it. Monari has shown that the ureter of a dog may be dissected from its outer vascular sheath for a distance of 12 or 13 cm., and if the operation is done carefully and it is placed back in the sheath and the above directions are followed, a fistula will not result; but when a drain separates a portion of the ureter from its sheath a fistula occurs.

The importance of the above has been emphasized by other writers. Undoubtedly many post-operative fistulae would not have resulted had these precautions been taken.

#### LIGATION OF ONE URETER AS AN AID IN THE MORE EXTENSIVE OPERATIONS FOR CARCINOMA OF THE CERVIX.

Landau,<sup>10</sup> in a combined abdominal and vaginal hysterectomy for carcinoma of the cervix, found it necessary to resect the lower 5 cm. of the right ureter, which was surrounded by carcinoma. On account of the length of the operation and the difficulties of an uretero-vesical implantation, due to the amount of the ureter resected, he tied the renal end of the ureter and dropped it, intending later to remove the kidney. The case was later more fully described by Weinreb.<sup>11</sup> The patient was seen six months later, apparently in the best of health, without any evidence of a return of the growth or of the formation of a tumor mass in the kidney region. Landau, on account of the favorable results of this case and of the cases of ligation of the ureter for surgical injuries to that organ reported by Bastianelli,<sup>12</sup> Futh<sup>13</sup> and Phaenemenow,<sup>14</sup> suggests that this procedure may enable one to remove carcinomatous uteri which would otherwise be considered inoperable.

I have been able to find in the literature but one other instance of intentionally tying the ureter in order to excise the lower end of it in a hysterectomy for cancer of the cervix, that by Bardenheuer.<sup>15</sup> The patient recovered from the operation, but died eight weeks later from renal infection.

There are many instances of unintentional ligation of the ureter during hysterectomy for carcinoma, especially by the vaginal route. We have been able to diagnose but one such case, Gyn. No. 1134, in this hospital, and the diagnosis was made at autopsy, the patient dying on the fourth day. One cannot say how much the injury to the ureter had to do with the death of the patient. Such an injury is suggested after operation when pain in the kidney region and along the course of the ureter arises and there is known to be a possibility of such an injury. These symptoms are made even more definite when in addition renal infection occurs or insufficiency of the other organ exists. A cystoscopic examination and catheterization of the ureters will aid in the diagnosis. Stoeckel<sup>16</sup> has called attention to the great difficulty in the diagnosis of such injuries. For in the absence of infection there are often apparently no definite symptoms, or such as there are may be easily obscured by the symptoms following such an operation. The other kidney, if sound, can readily adjust itself to the additional work and prevent the threatened uræmia. Stoeckel claims that the fistula which may result, as a rule makes evident the diagnosis of the injury and not the symptoms resulting from the occlusion of the ureter. The unintentional ligation of the ureter may at times be diagnosed from definite renal symptoms; at other times from the formation of a fistula; and then again, discovered at autopsy. Nevertheless, it would seem that there must be many instances where the ureter has been accidentally tied and the patient has recovered and the convalescence was considered uneventful.

There are three contraindications to this procedure in any operation:

1. When an uretero-ureteral or an uretero-vesical implantation is possible.
2. When pyuria is present or the ligation takes place in the presence of infection.
3. When renal insufficiency exists.

In two successful uretero-vesical anastomoses referred to in this paper, 4-5 cm. of the ureter were sacrificed and the implantation was easily accomplished under very little tension, and yet the bladder was not dissected free, as has been done by Kelly,<sup>17</sup> or the kidney pulled down, as suggested by Bovee.<sup>18</sup> Kelly claims that by freeing the bladder and drawing it back toward the posterior part of the pelvis to meet the shortened ureter, a distance of from 3 to 5 cm. can be gained. So it would seem to me that it would be possible to implant the ureter into the bladder in nearly every case in which it was possible to remove the growth.

One must realize that the ligation of the ureter in hysterectomy for cancer is not done under strictly aseptic conditions. Therefore, there is the additional risk of renal infection or the formation of a ureteral fistula, or both. In cases where the ureter has been involved by the growth there must be considered the possibility of the infection of the tissue about the ureter, the ureter itself, or even the pelvis of the kidney, from organisms present in the necrotic cancerous tissue. Also, abdominal hysterectomy for cancer of the cervix is

accomplished under more or less danger of infection of the pelvis, although the use of the Wertheim clamps has greatly lessened this. The sufficiency of the other kidney must be considered in all operations where one kidney is sacrificed, whether it is done by nephrectomy or atrophy caused by the application of a ligature to the ureter.

The question arises when the ureter is injured in this or any other operation where an uretero-ureteral or uretero-vesical implantation is impossible, what should be done. If pyuria is present, the suturing of a ureter into a skin incision is probably the safest procedure. A nephrectomy may be done later if necessary. The anastomosis of one ureter into the other at present seems too difficult, and the results are too uncertain. The implantation of the ureter into the intestines is accompanied with too great a risk of renal infection. The substitution of a piece of the intestines to meet the deficiency, as suggested by Barbat,<sup>22</sup> is accompanied with less danger of renal infection. The implantation of the ureter in the skin incision as near the bladder as possible, with the view of later dissecting the bladder free to meet it, or the formation of a channel from a flap of the bladder wall to meet the deficiency, as described by Van Hook<sup>23</sup> and Boari,<sup>24</sup> offers valuable suggestions. The ligation of the ureter is apparently justifiable when necessary, but the ligated end *must* be placed beneath the skin so that any post-operative complications may be controlled. Should renal insufficiency manifest itself, then the ligature may be freed and the function of that kidney probably restored. In this respect the ligation of the ureter is preferable to nephrectomy. Should pyonephrosis occur one would have a means of relieving the condition. Of great importance should a leakage take place, due either to the slipping of the ligature or to necrosis of the ureter brought about by the ligature, then it could easily be recognized and an avenue for the escape of the urine formed. Fraenkel,<sup>25</sup> as the result of his clinical observation and animal experimentation, has urged the importance of this procedure.

I wish to take this opportunity to refer to a recent article of mine, "Ligation and Clamping the Ureter as Complications of Surgical Operations."<sup>26</sup> The effect of *complete* and *permanent* ligation of one ureter in animals, and the results in some of the instances where it has been done in man, as well as the finding of such injuries at autopsy, caused me to think that in the absence of *infection* and renal *insufficiency* such a procedure would usually give rise to little or no pain and would probably not be accompanied by any untoward symptoms. Therefore, I made certain statements, to this effect, which, although they may be true, are not justifiable in the present state of our knowledge of the subject. They were these:

"When only one ureter is occluded, the diagnosis is indeed very difficult, for in the majority of cases there are *no subjective symptoms*." "It may be said that *generally* pain (renal or ureteral) is not present when the ureter is completely occluded"; also that "Complete and permanent occlusion of the ureter in the absence of infection leads to

renal atrophy, etc." These conditions take place *usually* without any symptoms or evidence of constitutional disturbances, and probably without much shock."

One must remember, however, that the patient is unconscious for some time after the operation, and that the symptoms arising from such an injury could easily be obscured by those usually following such an operation, and also by the use of sedatives. In some of the cases reported the condition in the pelvis, which led to the injury of the ureter, may by compression have gradually caused a partial or complete atrophy of the kidney, as was considered in the cases reported by Bastianelli and Veit.<sup>20</sup> In such cases the ligation of the ureter would probably give rise to few or no symptoms.

#### RESECTION OF THE URETERS IN HYSTERECTOMY FOR CANCER OF THE UTERUS WHERE THERE HAS BEEN WIDE LATERAL EXTENSION OF THE GROWTH.

Hysterectomy for carcinoma of the cervix with resection of the lower end of the ureter and implantation of the ureter into the bladder when the vesical end of the ureter was found to be surrounded by the growth, has been accomplished with success by several operators. Penrose,<sup>27</sup> in July of 1893, was probably the first to do this in an abdominal hysterectomy. He employed a suture to draw the ureter into the bladder, a method suggested by the Van Hook<sup>28</sup> end-in-side uretero-ureteral anastomosis, from which the method described by me, as well as similar operations reported by others, have been developed. Schede,<sup>29</sup> in 1890, in a hysterectomy by the sacral route, resected a portion of the ureter and bladder wall which were involved by carcinoma and attempted to implant the ureter into the bladder, but failed. Westermarck,<sup>30</sup> in 1894, in a similar operation was successful.

Dr. Kelly<sup>31</sup> was probably the first, and, as far as I am able to learn, the only one, to resect the ureter and successfully implant it in the bladder by the vaginal route in a vaginal hysterectomy, March, 1899, Gyn. No. 6831. This case was erroneously reported as an abdominal hysterectomy and implantation. Previous to the ones referred to in this article, we have had in this hospital but one other instance of hysterectomy for carcinoma of the cervix with resection of the lower end of the involved ureter. This was done in January, 1900, by Dr. Kelly.<sup>32</sup> Gyn. No. 7510. During recent years other operators in this country and abroad have successfully resected the lower end of the ureter and implanted it in the bladder in hysterectomy for cancer of the uterus involving the ureter.

Chalot,<sup>33</sup> in 1896, advocated the preliminary ligation of both internal iliac arteries and the systematic transplantation of both ureters into the bladder if possible, otherwise into the rectum, in cases of cancer of the cervix of the uterus with wide extension of the growth. He reports a successful operation with implantation of the ureters into the rectum. One may find recorded, cases of the resection of ureters and their implantation into the bladder, as well as into the skin,



FIG. 1.—Gyn. No. 9903. Path. No. 6103. Natural size. In this instance the lymphatics were removed from the pelvic vessels from above downwards, together with the uterus, and undisturbed all the tissue lateral to the cervix from pelvic wall to pelvic wall, including the lower 4.5 cm. of the ureters; and the ureters were implanted in the bladder. By comparing this with the picture of the usual hysterectomy for cancer of the cervix, one can see what is gained by the more radical operation.

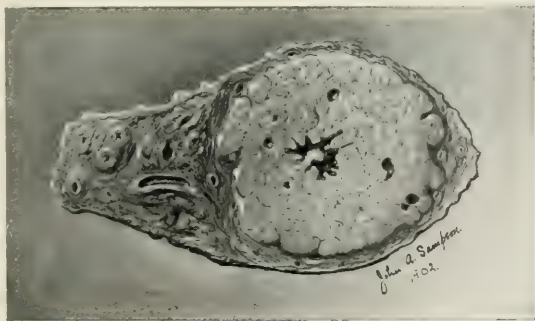


FIG. 2.—Gyn. No. 9860. Path. No. 6074. Natural size. Cross section, taken just below the level of the uterine artery, of a specimen from a hysterectomy for carcinoma of the cervix, where all the tissue between the cervix and pelvic wall, including the lower portion of the double ureter, was removed undisturbed, on the left side. On the right side the parametrium was cut through mesial to the ureter. The advantage gained by sacrificing the lower end of the ureter and removing undisturbed all the tissue lateral to the cervix, becomes very evident in comparing the two sides.

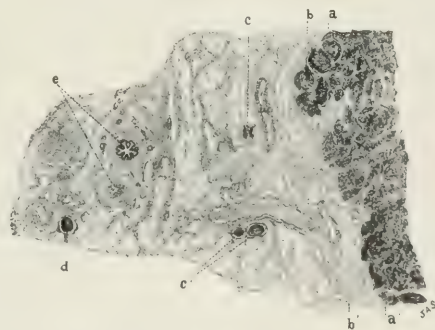


FIG. 3.—Section of the left parametrium, magnified twice, from specimen shown in Fig. 2.

*a-a'* is the outer border of the growth.  
*b-b'* is the outer border of the cervix.  
*e* is a cross section of the double ureter.  
*c-c'* and *d* are small lymph nodes having a diameter from .5 to 1.5 mm.

In this section cancer was found in the node marked *d*, which is posterior and lateral to the ureter. In other sections cancer was found in a node situated near *c'*. In a less radical operation some of the nodes containing cancer would have been left behind.



the pressure of the growth on the ureters. By studying the reports of cases of radical operations for extensive carcinoma of the cervix, we are able to judge of the possibilities of such an operation. In these cases the evident extent of the disease is the indication for the operation. It seems to me that the indications for such an operation in the so-called favorable cases, are just as evident; namely—

1. The high percentage of recurrences.
2. The involvement of the pelvic glands, apparently in at least one-third of the operable cases.
3. The inability at operation to diagnose to what extent the surrounding tissues are involved by carcinoma.

In addition one must bear in mind that the most radical operation is probably indicated more in the early than in the very advanced cases, for in the former there is the greater chance for a cure. I have emphasized the importance of the more radical operation. I wish now to emphasize these facts:

1. That a more radical operation is very difficult and is attended with a higher primary mortality than a less radical one.
2. That such an operation is but in the experimental stage, and the question of the route to use, as well as whether it is best to resect the lower ends of the ureters in the early cases, and many other features in such an operation, are problems which have not been solved.

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## NITROGEN EXCRETION IN PNEUMONIA, AND ITS RELATION TO RESOLUTION.<sup>1</sup>

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An unusually small number of crises and a large proportion of delays in resolution were occurring last fall in this Hospital, and several different methods of local treatment, such as ice bag and poultice to the chest were tried, with the view of shortening the course of the disease. Daily determinations of the total nitrogen excretion in each case by the Kjeldahl method were begun with the idea, that the daily surplus nitrogen excretion, above what would normally be excreted on the pneumonia diet, would be an index in direct proportion to the rapidity with which the involved lung was clearing.

This assumption was based: 1. Upon the fact observed by Svenson, Müller and others, that a post-critical nitrogen determination showed very marked increase in total daily nitrogen excretion, one case mentioned by Müller showing 28 grammes of nitrogen over what would normally be excreted on the same diet. This, as he took it, represented 175 grammes of albumin

or 800 grammes of pneumonic exudate which had been absorbed by the blood from the involved lung, and finally found its way into the urine. This hypothesis our observations have tended to confirm. 2. Upon our idea as to the course of events in consolidation and resolution of pneumonic lungs as drawn from standard pathologies. This may be briefly stated as follows:

The lung first becomes congested, or, as it is termed, engorged. This is followed sooner or later by consolidation, first in the form of red, and later of grey hepatization. The lung is now firm and solid, weighing from 1000 to 1500 grammes, according to Bollinger, or even 2000 grammes, according to Osler, more than it did in the normal state. This 1000 to 2000 grammes of exudate in favorable cases, softens and is gradually absorbed, finally leaving the lung clear.

Thus, supposing that the exudate absorbed by the circulation would appear in the urine as some nitrogenous extractive, and believing there were approximately 500 to 1000 grammes of exudate per lobe to be accounted for in this way,

<sup>1</sup>Read before the Johns Hopkins Hospital Medical Society, June 2, 1902.

it is evident that by knowing how much nitrogen was excreted daily above the normal for existing conditions, and also how much pneumonic exudate one gramme of nitrogen represented, we might easily estimate what proportion of the exudate was being excreted each day.

The variations in nitrogen content of the faeces were not considered, as the total daily nitrogen excretion from this source only averages about two or three grammes, according to the statistics of Riess, while the comparatively small amount of sputum relative to pneumonic exudate allowed of its being disregarded likewise.

It was hoped that one local application might cause the expected amount of nitrogen to be excreted sooner than another, indicating a more favorable condition for rapid resolution.

It was soon found, however, that while this calculation did very well for the small proportion of cases that resolved quickly (Charts No. I and IV) say in three or four days, that in cases of delayed resolution (Charts No. II and VII) quite as large an amount was excreted daily without seeming to make any impression on the condition of consolidation as shown by physical signs. In other words, whereas the quickly resolving case excreted its expected 1000 or 2000 grammes of exudate in three or four days, leaving the lung clear, on the other hand, the slowly resolving case would excrete its surplus of 200 to 500 grammes daily day after day and even week after week and still retain a flat note over the involved lung.

This of course made it out of the question that the daily nitrogen determinations would be even the most distant index of the rate of clearing. The determinations were continued however in view of the interesting questions they suggested and I report them here, without reference to the question of treatment for which they were undertaken, and which will be reported later. I wish to express my great appreciation of the interest and kindness of Dr. Emerson with whose encouragement this work was undertaken, and whose invaluable assistance in the nitrogen determinations made its completion possible.

Twenty-two cases in all were followed, the figures of which I append in full. All were from the men's wards. Determinations in all the cases, for one reason or another, could not be made daily through their whole course, but those that are incomplete agreed for the days they could be followed with the ones observed from onset to recovery. Thus, though some are incomplete, they are valuable as controls and supplements for the rest.

I was especially fortunate in obtaining two cases from the initial chill on, and the others included four crises, four cases of marked delay in resolution, two with continued fever, and two afebrile after the tenth day.

One case ended in empyema, and one case died. Several cases showed successive involvement of two or more lobes. The number of lobes involved varied from one to four, and period of resolution from three days to eight weeks.

These patients took about 6 to 8 grammes of nitrogen a day in the routine milk and albumin-water diet during the con-

tinuation of the fever, and after the temperature became normal about 10 grammes of nitrogen in the general soft diet. Other patients than the pneumonia cases excreted about 8 grammes of nitrogen daily with a milk and albumin diet and 9 or 10 grammes of nitrogen with a soft diet.

The question may be asked, can the surplus nitrogen excretion in these cases be considered as representing in greater part pneumonic exudate, as Svenson and Müller surmised, and as our observations tend to confirm; or is it to be accounted for merely by the fever, or by the leucocytosis? Against the latter view are opposed the following:

1. Although the results of various investigators tend to show an increased metabolism as indicated by increased nitrogen excretion in many cases with pyrexia, some of the results are conflicting, and although it is undoubtedly true that in many cases pyrexia and increased nitrogen excretion are coincident, yet these cases (Charts I and III) show definitely that a continued fever of 104 degrees, accompanied by a leucocytosis of 20,000, may persist for several days consecutively, with the patient excreting a normal or subnormal amount of nitrogen; and also that for weeks after both temperature and leucocytes are normal a surplus of ten to fifteen grammes of nitrogen may be excreted daily (Charts II and VII). The interesting experiments of Krehl and Matthes<sup>2</sup> on aseptic fevers in man and animals, also show conclusively that it is not the temperature *per se* that causes the increase in metabolism and increased nitrogen excretion. They found that injections of certain poisons, such as iodine, silver nitrate and albumoses, may cause a rise in temperature or may not; but, in either case, the nitrogen output was increased, showing that it is the poisoning and not the temperature that causes the surplus nitrogen.

Again, the statistics of Riess<sup>3</sup> on nitrogen excretion in typhoid show one case that on the ninth and tenth days of the disease excreted an average of 16.4 grammes of nitrogen each day with a maximum temperature of 104.7°, and yet on the sixteenth and seventeenth day of disease passed an average of 16.5 grammes of nitrogen with a temperature of 100.2°, thus showing a difference of only one-tenth gramme of nitrogen with a difference in temperature of 4.5°. This same case on the twelfth and thirteenth days of the disease under treatment with continued bath passed twenty-three grammes of nitrogen per day, with an average temperature of 101.5°, thus treatment with hydrotherapy causes a difference of seven grammes of nitrogen per day, whereas 4.5 degrees of temperature caused but one-tenth gramme difference. So although pyrexia and leucocytosis may be accompanied by increased nitrogen output, no inevitable association nor causal relation can be considered proven.

2. In a pneumonia case with one lobe involved we know that 500 to 1000 grammes of exudate must be gotten rid of in some way and our observations on two cases in which a single lobe resolved in several days showed during those days

<sup>2</sup> Archiv f. Ex. Path., vol. 40.

<sup>3</sup> Archiv f. Ex. Path., vol. 22, p. 151.

a total surplus nitrogen excretion of 440 grammes and 1070 grammes respectively. This leaves but little to be accounted for by either fever, leucocytosis or toxæmia.

3. The surplus nitrogen, although showing no definite relation to the temperature, does show a very close coincidence with physical signs, that is after resolution once begins. Thus we find that after the first few days, whenever the lung by clinical signs shows consolidation, we get surplus nitrogen, and as soon as these signs are clear we have normal nitrogen excretion.

The history of a pneumonia case from the point of view of nitrogen excretion seems to be as follows:

During the first day or so following the initial chill the nitrogen output is below normal, as we might expect when we consider that is short while 500 to 1000 grammes of exudate per lobe is stored in the involved lung at the expense of the rest of the body. It is in this way that Bollinger explained the oligæmia to which he called attention in pneumonia.

From about the third day on we find a gradual rise in nitrogen excretion corresponding, as I interpret it, in greater part, to beginning resolution and absorption of the liquefying exudate, plus probably some excretion of destroyed tissues retained in other parts of the body. This finally comes to a maximum in two more days, and if there is no further involvement, and the lung is clearing well, the nitrogen excretion returns rapidly to normal.

There are variations from the above picture of what may be taken as a type of the average favorable case.

In one case evidences of beginning resolution did not come until the sixth day. This was an old man of sixty with an alcoholic history (Case 3). In another (Case 12) the rise in nitrogen output came on the second day with involvement of a second lobe. This was after one day's interval without fever, physical signs, or surplus nitrogen. In other words, the patient was well for one day, then suffered involvement of the opposite lower lobe which began to resolve on second day, and was practically clear and the patient well on the sixth day.

The greatest variations are found in time required for resolution, one case requiring three, another six, and a third over eight weeks.

It was in such cases of delayed resolution that the remarkable quantity of surplus nitrogen was excreted. One case (See Chart II, Case 16) during the first thirteen days of admission excreted a surplus amount of nitrogen which would represent the weight of exudate in four consolidated lungs, yet this patient's lung was not entirely clear on the twenty-fourth day of admission, and but one lobe of one lung was ever involved. Temperature had been normal since the eighth day.

A second case (Case 5) also excreted the equivalent of four consolidated lungs, and this during the first twenty-four days of admission, and the chest had not cleared on the sixtieth day, and in this case but one lung was ever involved, and the temperature had been normal since the seventeenth day. Several other of the cases during delay in reso-

lution excreted much more nitrogen than could be accounted for by the original quantity of exudate. To account for this brings us back to the same difficulty that made the nitrogen determinations useless as an index to the rate with which the lung was clearing. Now if, as we believe, the total surplus nitrogen in these cases still represents, in great part, absorbed pneumonic exudate, and exceeds by many fold the original area of consolidation, the only supposition left tenable is, that the pulmonary condition in these cases is not, as we took for granted, a passive status quo, waiting for weeks to be carried away, but a continually progressing cycle of formation, liquefaction, and absorption of pneumonic exudate.

If we look at the question in the light of recent work that has been done by Müller<sup>1</sup> on resolution in pneumonia, it makes it all the more improbable that the hepatized lung should remain filled with the same consolidated exudate at the end of a couple of months as it had at first. He found that a lump of lung in the stage of grey hepatization, if rendered sterile to exclude bacterial action, and kept at the same temperature as the body, would resolve invariably and completely in a few days. This he showed was due to the presence of autolytic ferments derived probably from the cellular elements of the exudate.

Why should such a lung, if left in the body, remain unchanged? I cannot conceive that it could, except with the rather chimerical assumption of the formation of anti-ferments. Now if it does liquefy and does not clear, it must be because the liquid is retained in the lung. But we know this is not the case; for,

1. When such cases come to autopsy the lung is solid, as in the case Grissold described in which at autopsy on the 60th day the affected part showed a condition not unlike that of the acute stage. (Osler.)

2. We obtain the equivalent of that liquid several times over in the urinary excretion.

This, of course, throws no light upon the course of the symptomatic side of the picture, and only emphasizes the fact long recognized that the pulmonary condition bears no definite relation to the clinical symptoms. An explanation of defervescence and a drop in leucocytes with continued local conditions, must probably be postponed with many similar problems to the day when the conceptions of specific antibodies are elucidated.

The fact that many of these cases where the lung remains solid are afebrile and show no leucocytosis is no contra-indication to a continued local process. For many other morbid conditions involving pus formation become afebrile and without leucocytosis after surgical interference or spontaneous evacuation, although the local inflammation, as evidenced by copious pus formation, continues. Then, besides, in pneumonia we so often see a patient with violent fever and rapid heart, and seemingly on the verge of dissolution, several hours later sleeping quietly, or asking for food, apparently well. It is scarcely conceivable that an inflammation which

<sup>1</sup> Verh. d. Naturforsch. Gesellsch. in Basel. Band XIII, Heft 2.

can produce 1000 or 2000 grammes of exudate in a couple of days, would come to a complete standstill in several hours.

The case ending in empyema is of special interest in that it suggests that nitrogen determination may be of diagnostic value in doubtful cases with continued flatness. In this case with a flat note over the left chest on the 17th day the nitrogen excretion was about normal, whereas in every case where a continued flat note was due to delayed resolution the nitrogen excretion was much above normal. The explanation of this would seem to lie in the different capacity of the pulmonary tree and the pleural sac for absorption.

In view of Müller's suggestion that the leucocytes might furnish a large part of the ferment concerned in the liquefaction of the exudate, I was interested in comparing the leucocytosis curve with that of the nitrogen excretion.

His supposition of the importance of the leucocytes in this process was drawn from the knowledge that pus does contain a proteid-splitting ferment, and from the microscopic picture of the stages of resolution. He pointed out that in the stage of grey hepatization where resolution first begins the microscopic picture shows an increase in leucocytes.

From another point of view I find an analogous phenomenon. The leucocytes in the blood reach their maximum a day or two before the maximum excretion of nitrogen; and in cases where the nitrogen output soon reaches normal the curve of leucocytosis follows it closely, though the temperature may have fallen a day or so previously.

The case mentioned above where increased nitrogen out-

put did not appear until the seventh day, had, previous to that time a leucocytosis of about 17,000; on the second day after, with a nitrogen output which had increased 500 fold in three days, the leucocytosis was 28,000.

All of which tends to substantiate Müller's idea that the leucocytes play an important part in the process of resolution. That there is no leucocytosis during the latter part of many cases of delayed resolution is difficult of explanation, but not more so than the similar condition so frequent in surgical cases as mentioned above, where, after operation, a continued pus formation goes on after the leucocytes are normal.

To sum up:

1. In cases of pneumonia a surplus amount of nitrogen must be excreted during the days of resolution that will correspond at the least to the original quantity of exudate poured into the involved lung. In most cases there is more, the rest representing in great part a continuation of the formation and an absorption of inflammatory exudation, plus other tissue destruction.

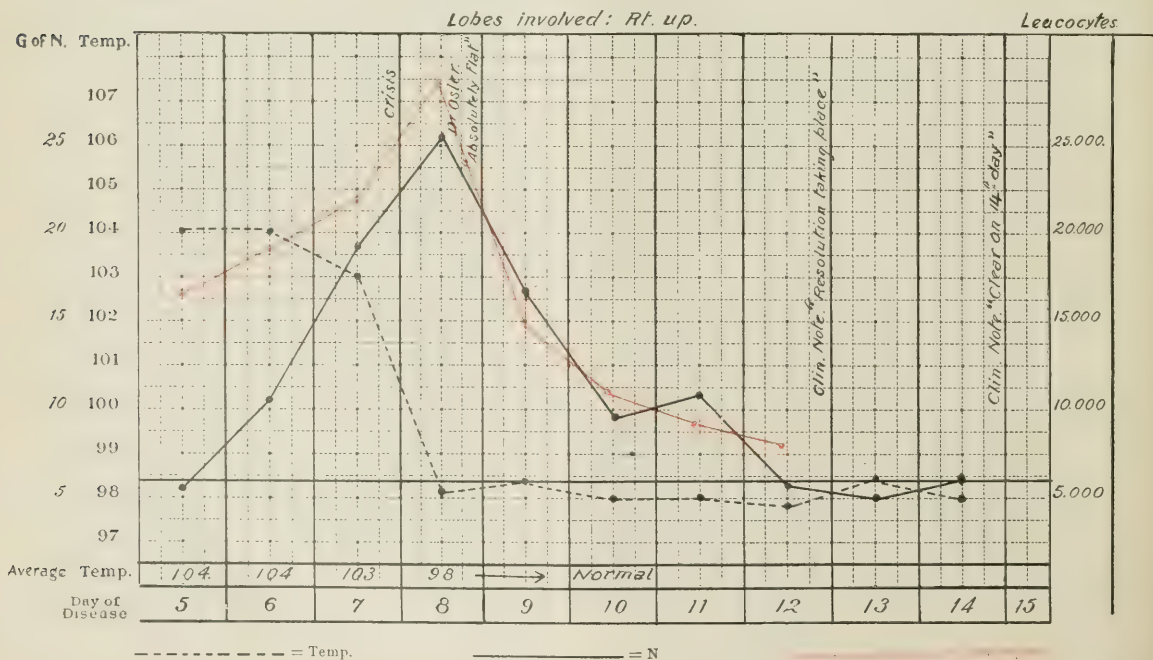
2. In cases of marked delay in resolution the continued high nitrogen output indicates a continuation of the local inflammatory process, so that in those cases of several months' persistence we might speak of a chronic pneumonia.

3. In cases of rapid resolution the leucocytosis curve follows the curve of nitrogen excretion with a very striking parallelism, and would seem to point to a causal relation between leucocytes and resolution.

CHART I.

CRISIS WITH PROMPT RESOLUTION.

CASE 3.



Total surplus N represented 1,540 G exudate.

CHART II.

LYSIS WITH DELAYED RESOLUTION.

CASE 16.



CHART III.

CRISIS WITH DELAYED RESOLUTION.

CASE 2.

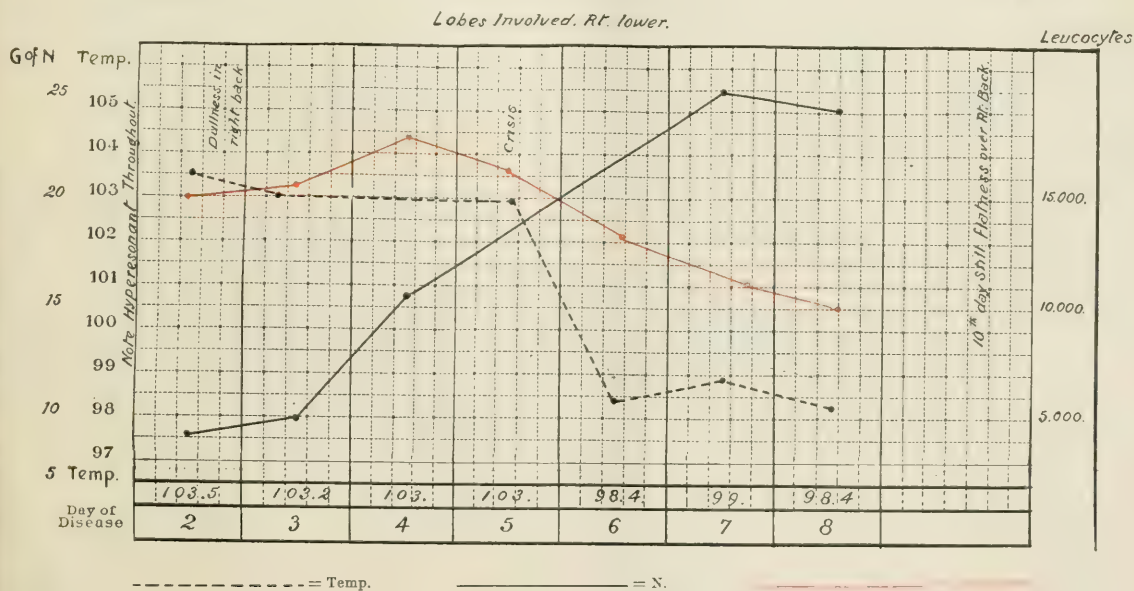
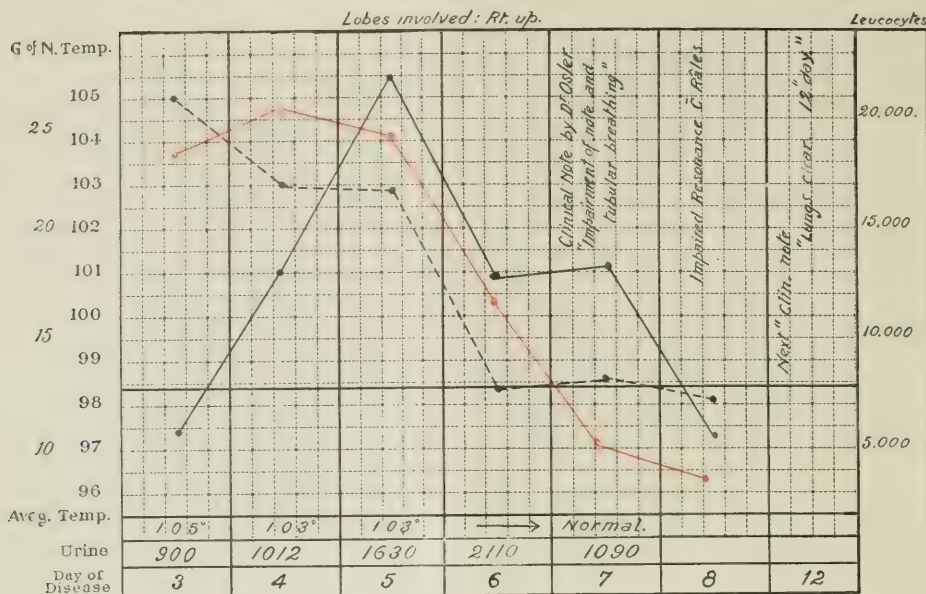


CHART IV.

CRISIS WITH PROMPT RESOLUTION.

CASE 18.



--- = Temp.

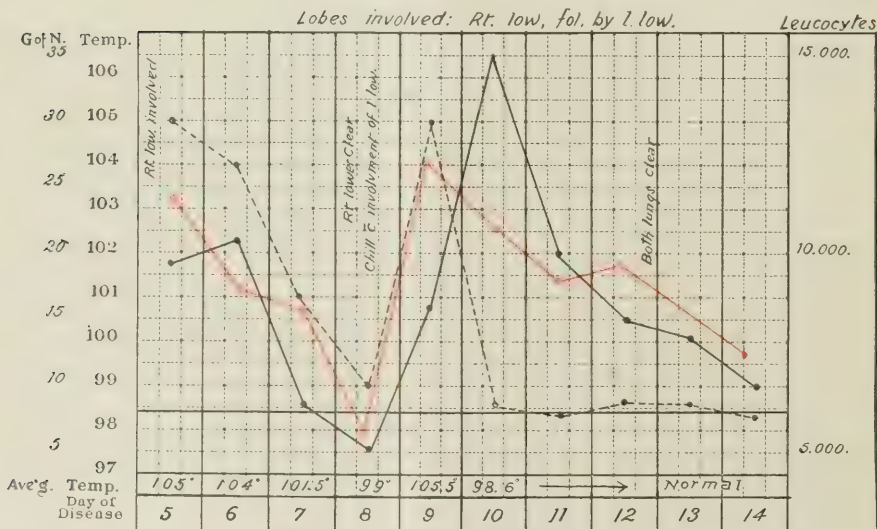
— = N.

Total surplus N represented 1,070 G of exudate.

CHART V

CRISIS WITH PROMPT RESOLUTION.

CASE 12.



--- = Temp.

— = N.

Nitrogen excretion for 2d lobe = 440 G exudate.

CHART VI.

CRISIS WITH PROMPT RESOLUTION.

CASE 14.

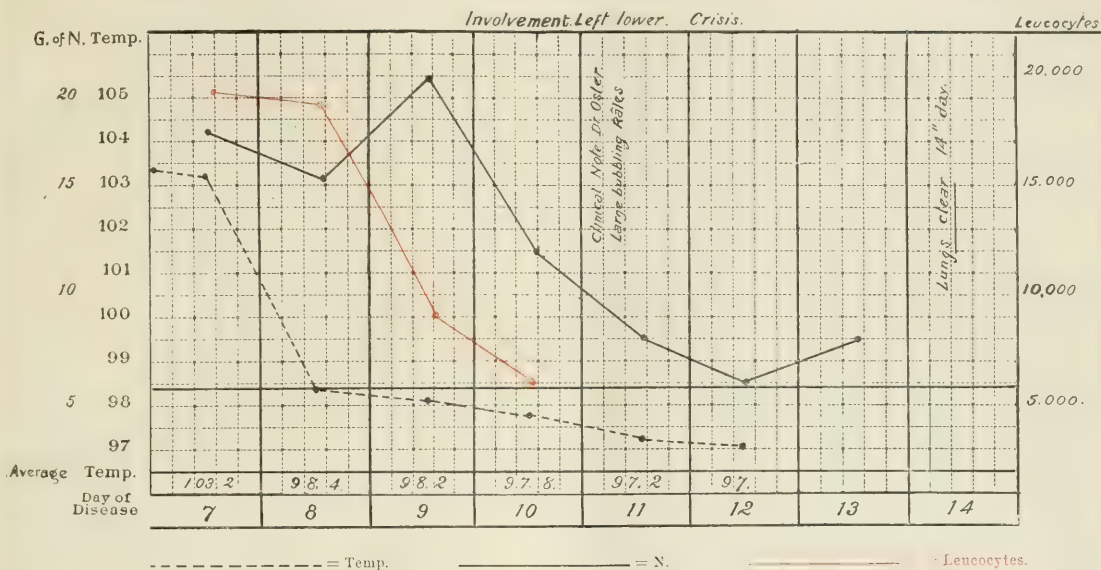
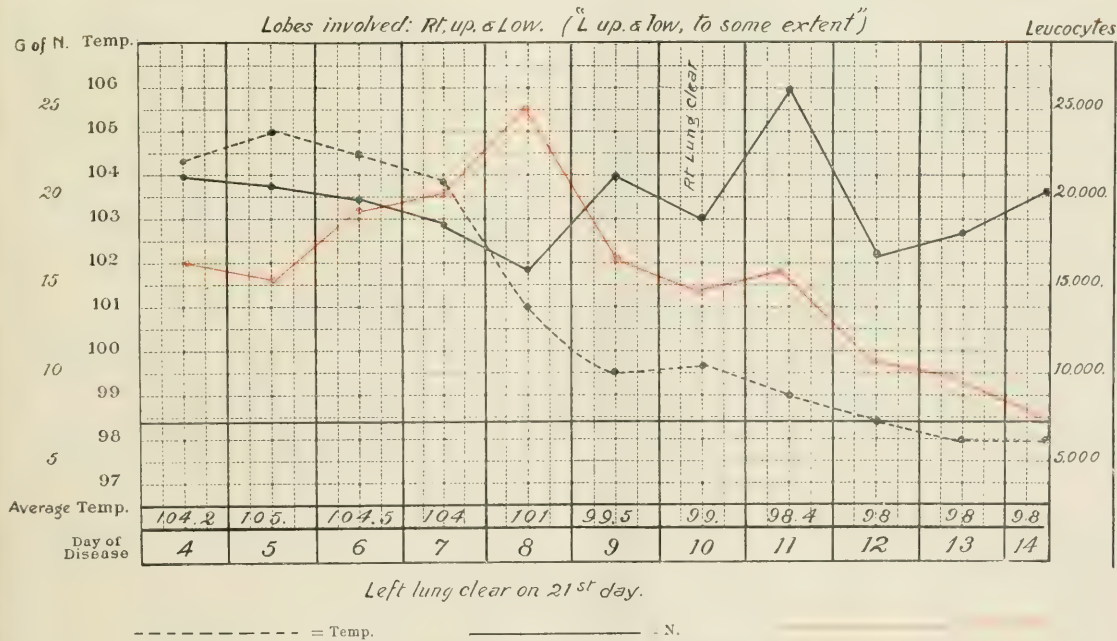


CHART VII.

LYSIS WITH DELAYED RESOLUTION.

CASE 1.



Total surplus N represented 2,600 G exudate, to 14th day.

## CASE 1.

Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
4	1200	21.3	16,300
5	1310	20.7	15,000
6	1240	20.2	18,000
7	1640	18.9	19,000
8	1160	16.5	25,000
9	1600	23.2	14,000
10	920	18.6	15,000
11	1440	27.8	....
12	1280	15.5	11,000
13	1110	16.2	....
14	1070	19.5	8,000

L. lung clear. }  
Temp. normal. }

This was a very severe case of lysis with both lungs involved on admission. Resolution was slightly delayed. Lungs clear by physical signs on the 21st day. Total surplus N to 14th day represented 2.600 G exudate. See Chart VII.

## CASE 2.

Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
Dullness in rt. back .....	2	540	9.5
	3	550	9.8
	4	840	15.6
Crisis .....	5	1060	17.0
	6	1660	....
	7	3240	24.9
	8	2175	23.2

Crisis with delayed resolution. On admission, 1st day of disease, note was hyper-resonant throughout chest. On 2nd day dullness in rt. back. On 10th day still flatness in rt. back. Clear on 23rd day. Involv. rt. lower. See Chart III.

## CASE 3.

Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
5	320	5.5	17,000
6	460	10.6	19,000
Crisis .....	7	1050	19.8
	8	1380	25.6
	9	1140	17.2
	10	1440	9.8
	11	1660	13.8
	12	750	5.8
	13	....	....
	14	....	....
	15	1000	5.4
	16	1140	6.3

Crisis with prompt resolution. Almost entirely clear on 13th day. Involvement rt. upper. See Chart I.

## CASE 4.

Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
3	780	11.2	13,000
4	930	12.3	14,000
5	670	9.6	22,000
6	680	10.2	25,000
7	610	19.9	21,000
8	1060	15.2	28,000
9	1040	21.1	23,000
10	1520	....	....
11	1280	12.5	22,000
12	790	11.2	13,000
Temp. nor. ....	13	1020	13.1
	14	890	12.2
	15	965	....
	16	920	....

Day of disease.	Cc. urine in 24 hours.	G of N in 24 hours urine.	Leucocytes.
17	1030	....	....
18	780	11.2	....
19	1290	11.5	....
20	1380	....	....
21	580	9.2	....
22	985	10.1	....
23	660	....	15,000
24	780	13.1	13,000
25	1230	16.6	....
26	640	....	12,000
27	970	14.2	....
28	....	....	9,000

Lysis with delay in resolution. Clear on 31st day.

Involv.—Left lower; later right lower.

## CASE 5.

Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
4	1000	8.5	26,000
5	1040	11.5	....
6	1040	....	6,000
7	1500	21.0	8,700
8	1860	29.6	14,100
9	2440	37.5	22,000
10	2135	36.3	17,000
11	1670	32.0	....
12	1620	26.5	18,000
13	2200	32.8	15,700
14	1620	24.1	10,600
15	1440	21.2	....
16	1450	21.3	....
17	1450	24.6	....
Temp. nor. ....	18	1180	20.6
	19	2620	22.0
	20	1960	19.3
	21	1360	17.1
	22	1220	12.9
	23	1460	17.4
	24	1180	15.9
	25	1330	18.1
	26	1320	15.9
	27	1890	15.2

Lysis with marked delay in resolution. Not quite clear on 60th day.

Involv.—Left lower and upper. Surplus N excretion for 23 days represented 7,400 G exudate.

## CASE 6.

Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
4	720	25.2	8,000
5	1260	27.5	5,000
6	1150	22.6	9,000
7	1080	24.1	12,000
8	1310	27.1	....
9	1520	28.2	13,000
10	980	19.5	11,000
11	900	18.7	....
12	1100	20.5	11,000
13	....	....	....
14	910	17.1	14,000
15	800	15.3	14,000
16	630	14.1	....
17	420	9.5	14,000
18	930	8.1	....

Case ending in empyema. Pus drawn on 19th day.

It is noteworthy that with the side flat on 17th day there was approximately a normal N excretion. Involv. l. lower.

## CASE 7.

	Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
	4	1600	26.8	15,000
	5	1500	25.4	8,000
	6	2220	35.7	5,000
Invol. of low. lobe.....	7	880	15.8	....
	8	1160	22.7	6,000
	9	2720	28.6	10,000
	10	2790	15.4	11,000
Up. lobe clearing	11	1020	9.6	13,000
	12	1180	11.7	9,000
	13	1800	25.5	9,000
	14	2340	30.7	9,000
	15	2400	25.5	8,000
	16	1860	26.0	7,500
	17	1800	42.4	....
	18	1660	19.7	....
	19	1140	14.9	....
	20	1320	16.6	....
	21	1520	17.0	....
	22	1000	10.0	....

Severe case, ending by lysis on 10th day. Resolution delayed. Not entirely clear on 25th day. Rt. up. involved on admission, clearing on 12th day. Rt. low. involved about 7th or 8th day.

The rise and decline in N excretion corresponding to the successive clearing and involvement of the two lobes is well shown. Surplus N represents 6000+G exudate.

## CASE 8.

	Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
	6	1185	23.2	10,000
	7	1140	19.7	....
	8	1240	22.9	37,000
	9	1245	23.2	40,000
	10	1105	25.1	18,000
	11	775	23.9	20,000
	12	770	18.6	16,000
Temp. nor.....	13	780	15.1	....
	14	670	14.2	....
	15	....	....	12,000
	16	....	....	9,000

Lysis with only slight delay in resolution. Clear on 15th day. Involvement: Left upper and lower lobes.

## CASE 9.

	Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
	4	500	9.3	25,000
	5	1080	21.8	20,000
	6	1400	28.9	30,000
	7	1260	22.1	31,000

Death on 8th day. From the increase in N excretion it would appear that absorption had been taking place since 5th day. Involvement: Right upper and lower lobes.

## CASE 10.

	Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
Crisis .....	5	1120	18.2	10,000
	6	840	18.4	7,000
	7	860	19.7	4,500
	8	905	19.2	5,000
	9	630	13.4	....

Crisis with slight delay in resolution. Clear on 14th day. Involvement: Left lower.

## CASE 11.

	Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
	3	920	14.9	13,650
	4	1170	....	10,700
	5	1270	23.5	....
	6	1200	27.2	....
	7	1240	28.9	8,000
Temp. nor.....	8	860	19.0	....
	9	940	20.1	10,000

Lysis with delayed resolution, not quite clear when discharged on 20th day. Involvement: Left lower.

## CASE 12.

	Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
	5	1372	19.1	11,600
	6	1500	20.0	8,200
Rt. lung clear.	7	1320	7.02	8,000
Chill with invol. of l. lung.....				
Signs at l. base.	8	1130	5.5	5,500
	9	1440	16.0	12,100
	10	830	16.3	10,500
	11	1820	35.6	9,000
	12	1506	20.0	10,000
	13	1250	15.31	6,000
Clear.....	14	1520	14.3	....
	15	1380	10.0	....

Successive involvement of two different lobes, first terminating by lysis, second by crisis, both resolving promptly. See Chart V.

## CASE 13.

	Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
	5	1160	25.4	12,600
	6	1500	36.4	6,000
	7	1340	31.4	7,000
	8	1380	31.5	6,000
	9	1370	32.6	....
	10	1090	29.0	....
	11	960	18.9	....
Temp. nor.....	12	....	....	....

Lysis with some delay in resolution. Clear on 15th day.

Invol.—Rt. up. and low.

## CASE 14.

	Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
	7	900	18.2	19,000
Crisis .....	8	760	15.3	18,700
	9	1000	21.9	9,000
	10	560	11.5	6,000
	11	470	7.1	....
	12	400	7.6	....
	13	410	6.7	....

Crisis with prompt resolution. See Chart VI.

Invol.—L. lower.

## CASE 15.

	Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
Fall in temp. } began.....	7	2000	26.3	24,800
	8	2010	23.2	24,000
	9	1860	21.5	16,300
	10	1160	16.2	23,200
Temp. nor.....	11	1640	18.8	19,100
	12	1340	15.2	18,800

Lysis with moderate delay in resolution. Clear on 15th day.

Invol.—Rt. upper.

## CASE 16.

Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
4	1470	28.1	20,000
5	2160	30.2	15,000
6	1960	32.9	17,000
7	1080	26.6	28,000
8	1560	24.8	45,000
9	2625	37.3	44,000
Temp. nor. .... 10	2380	30.8	30,000
11	2460	28.6	14,000
12	2100	29.3	8,000
13	1840	25.6	10,000
14	1220	23.7	7,000
15	1400	24.0	7,000
16	1420	24.2	....
17	1070	23.2	Normal.
18	1050	23.5	

Lysis with delayed resolution. Not entirely clear on 28th day.

Involvement.—Left lower. Surplus N from 4th to 18th day represented 7,100 G exudate. See Chart II.

## CASE 17.

Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes
5	1400	19.0	14,000
6	1460	23.6	16,000
7	2060	33.4	11,250
8	2050	26.9	....
9	1750	23.1	23,000
10	1690	23.6	18,500
11	2340	23.4	12,000
12	2460	31.5	15,600
13	2510	14.3	16,200
14	3205	14.3	5,830
15	2290	17.6	....
16	1490	15.6	12,000
17	1305	16.6	15,000
18	1230	.	9,500
Temp. nor. .... 19	1160	19.1	8,200

Lysis with marked delay in resolution. Not clear until 48th day.

Involvement.—Whole of left lung, and right lung to slight degree.

## CASE 18.

Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
3	900	11.3	18,000
4	1020	17.9	20,000
Crisis . . . . . 5	1630	26.9	19,000
6	2019	17.7	11,000
7	1090	18.6	3,000
8	770	11.9	4,000

Crisis with prompt resolution. Perfectly clear on 12th day. See Chart IV. Involvement.—Rt. up. lobe.

## CASE 19.

Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
3	2290	10.8	15,000
4	....	....	21,000
5	2000	12.0	15,000
6	1400	20.9	....
Temp. nom. .... 7	1180	16.5	14,000
8	960	14.5	....
9	820	13.2	15,000

Lysis with slight delay in resolution. Clear on 16th day.

Involv.—Left lower.

## CASE 20.

Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
6	1640	17.9	19,000
7	1680	19.6	18,000
8	1780	37.1	20,000
Temp. nor. .... 9	1780	26.1	21,000
10	1150	17.5	21,000
11	1150	20.5	....
12	1050	19.3	18,000
13	990	19.4	12,000
14	1140	19.7	....
15	810	....	10,000
16	800	13.5	....
17	740	10.4	....

Lysis with slight delay in resolution. Clear on 18th day.

Involv.—Rt. and left lower lobes.

## CASE 21.

Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
5	1190	9.7	11,000
6	760	12.6	8,000

Lysis with prompt resolution. Clear on 12th day.

Involv.—Rt. up.

## CASE 22.

Day of disease.	Cc. urine in 24 hours.	G of N in 24 hrs. urine.	Leucocytes.
7	1780	19.1	15,000
8	1270	37.9	14,000
9	1170	31.0	21,000

Lysis with slight delay in resolution. Clear on 15th day.

Temp. normal on 13th day.

Two incomplete cases.

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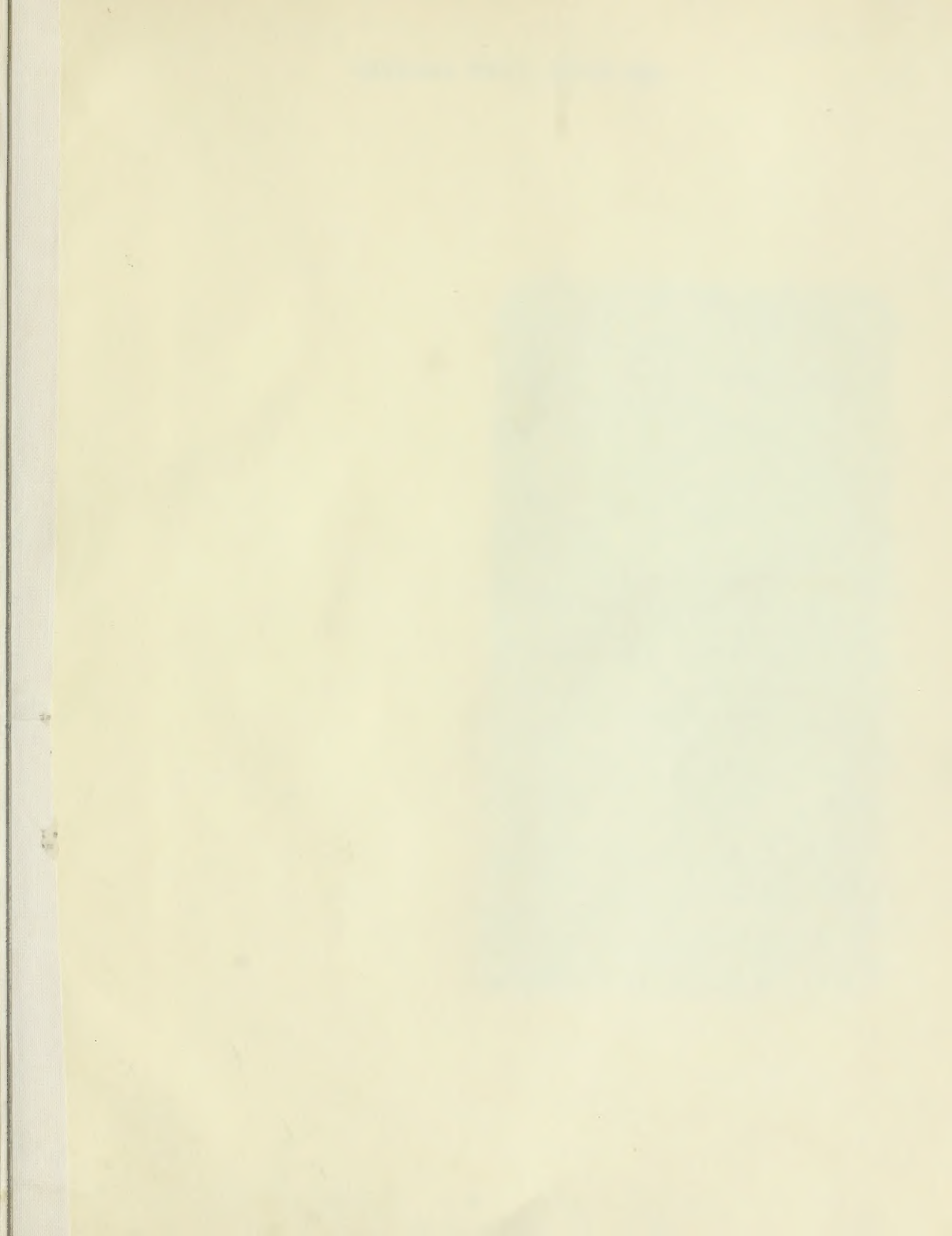
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